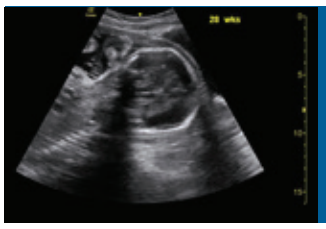

ULTRASOUND

Not So FAST!

SEE PAGE 12

STI TESTING

Chlamydia and Gonorrhea Testing Best Practices

SEE PAGE 15

EQUITY EQUATION

Combat Microaggressions

SEE PAGE 19

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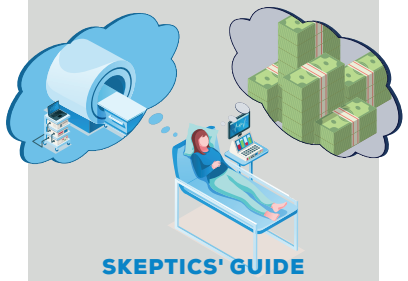

SKEPTICS' GUIDE TO EM

"CAN WE PAY YOU $100 TO NOT GET A CT?"

SEE PAGE 23

CAREER TRANSITION

CHANGING PATHS FROM ACADEMIA TO BUSINESS

SEE PAGE 10

FIND IT ONLINE

For more clinical stories and practice trends, plus commentary and opinion pieces, go to:

www.acepnow.com

A NEW JOURNAL JOINS THE FAMILY

JACEP Open, ACEP's newest publication, launched this month

Over the past year, ACEP has been developing a new journal to join the *Annals of Emergency Medicine* and *ACEP Now* as flagship publications of the College. The new journal, entitled *JACEP Open* (*The Journal of the American College of Emergency Physicians Open*), published its first articles in December 2019 and will debut its first issue in February 2020. Its inaugural Editor in Chief is Henry Wang, MD, MS, professor and executive vice-chair of research in the department of emergency medicine at the University of Texas Health McGovern Medical School in Houston. He is a prolific researcher and editor who has served as deputy editor for the *Annals of Emergency Medicine*.

Dr. Wang recently sat down with *ACEP*

CONTINUED *on page 16*

EM CASES

IV vs. PO

Are IV antibiotics better than oral antibiotics for common ED infections?

by ANTON HELMAN, MD, CCFP(EM), FCFP

The perceived need for intravenous antibiotics drives many hospital admissions. In a sense, the decision to administer IV antibiotics instead of oral formulations represents a line in the sand between infections we are worried might kill a patient and ones that won't.

But for the vast majority of common infections we treat in the emergency department, oral antibiotics should actually be preferred over IV antibiotics when efficacy, safety, efficiency, and cost are taken into account together. My goal is to convince you to correctly choose oral antibiotics more often. I believe this will lead to fewer admissions, fewer hassles, and less suffering for our patients.

Of course, there are various physiological arguments that support oral antibiotics being theoretically as effective as IV antibiotics. But I know that, in order for us to

CONTINUED *on page 24*

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MEDICOLEGAL MIND

Discovery and Deposition Primer

PAGE 20

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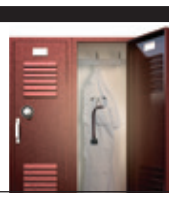

SEND YOUR THOUGHTS AND COMMENTS TO ACEPNOW@ACEP.ORG

EDs Can't Fix Overcrowding Alone

[In response to "ED Overcrowding " by Anton Helman, MD, CCFP(EM), FCFP (Nov. 2019)], the case of Brian Sinclair would indeed be dramatic were it not for the fact that this has happened in other emergency departments all over the world. Let me be clear: There are indeed *known* solutions to the problem of ED crowding. Implementing all the CQI and Lean efforts within the ED do not solve this problem; they are diversions from the real problem. We are, in effect, "polishing shiny toys" to show we're doing our part. These efforts, however, create an impediment to real solutions by creating an expectation that yet one more internal solution can solve this problem. Thus, we put providers at triage, implement guidelines, and blame ourselves. You have delays in radiology reads? Well, order fewer tests. You have too many admissions? Admit fewer. In short, only when the ED is "perfect" and has polished all the shiny toys will there be pressure outside the ED. So, go at it.

There are three known solutions that increase capacity and reduce boarding: smoothing of electives, early discharges, and increasing the number of weekend discharges. The full capacity protocol is a "failure" protocol to be used in times when beds can't be found. Not only do these solutions work, but they ultimately benefit patients, staff, physicians, and the financial health of the institution. In one institution, smoothing resulted in a $130 million improvement in the bottom line with elimination of boarding. In another institution, enhancing weekend discharges not only reduced boarding from an average of 30 patients to zero, but was so effective that a 30-bed inpatient unit was closed; this effort represented a $70 million positive improvement for the hospital. Discharge before noon at one institution dropped their O/E by 0.8, which represents a massive financial gain. I mention the very substantive financial gains because "something terrible will happen to a patient" sadly and obviously hasn't rung anyone's bell.

If these things are so effective, why aren't they done everywhere? Notice that the trio of solutions to improve capacity requires a change in physician behavior. The physician doesn't have to work harder (in fact, their job becomes easier), they just have to work *differently*.

So, who's going to make them? That's where the solutions fall apart. Successful institutions have all been characterized by strong leadership, leadership that demanded these changes and kept at it until there was success. One should ask, Why are there so few of them?

If you're working in a place where they're "working on it," meeting about it, looking at data every month to see if things change, and suggesting another project for the ED to take on as the problem of boarding continues to worsen—well, welcome to our world. When CMS, The Joint Commission, or your health department comes to visit to assure that safe care is being rendered and has to squeeze by the patients in your hallways in the most obvious of unsafe circumstances, and you receive a citation for a fire extinguisher past its expiration date—well, welcome to our world.

(Asa) Peter Viccellio, MD, FACEP
Stony Brook, New York

EM Remembers Dr. Peter Rosen

Thanks for the wonderful biography of a legend in EM. Peter was on the ABEM Board and as such could not take the exam until he had been off the Board for, I believe, five or 10 years. When he got around to taking the oral, as was the practice, all oral examiners had the ability to cross off candidates that they felt they had a conflict of interest. With Peter's cantankerous reputation, NO ONE wanted to be his examiner. I knew him, of course. Ben Munger, CEO of ABEM, came to me the first day of the exam and told me I HAD to test Peter in the double scenario. I reluctantly agreed.

When Peter came into my room, I felt like standing and saluting (think George Patton to imagine the moment). One of the scenarios involved pancreatitis, and one of the critical points was to order an amylase. He did a perfect exam and ordered his KUB and lab but did not mention amylase. Now what do I do? "Is there anything else you would like, Dr. Rosen?" "No thanks," was the answer. When it later came time to reveal his X-ray and lab results, the amylase was on a separate page that I withheld. He asked, "Where's my amylase?" "You didn't order one," was my answer. "You caught that, eh? I would like to order one now." Shortly, he got his result. Catastrophe avoided—I would have had to fail Peter Rosen.

John C. Johnson, MD, FACEP(E)
Valparaiso, Indiana

Dr. Rosen was the one person I have always respected and admired. My only meeting with him was many decades ago when he administered my oral board exam.

Thank God I chose to study his textbook for my oral exam.

Paul Orcutt, MD, FACEP
Oklahoma City

Correction

The December issue's "Residency Spotlight" listed the incorrect program director for the University of Vermont Emergency Medicine (UVM EM) program. Dr. Rich Bounds is the inaugural program director. In addition, UVM EM has just announced its first fellowship, a one-year medical education fellowship. Dr. Tabitha Ford, graduating from the University of Utah in June 2020, will join the leadership team as the first medical education ED fellow, and Dr. Bounds will serve as the fellowship director.

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In the emergency department, both safety and efficacy matter

For appropriate patients with DVT/PE, consider **ELIQUIS** at discharge

DVT=deep vein thrombosis; PE=pulmonary embolism.

INDICATION

ELIQUIS is indicated for the treatment of deep vein thrombosis and pulmonary embolism.

IMPORTANT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events.
If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.
Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

Please see additional Important Safety Information and Brief Summary of Full Prescribing Information, including **Boxed WARNINGS,** on adjacent pages.

AMPLIFY[1,2] Study Design

A randomized, double-blind, phase III trial to determine whether ELIQUIS was noninferior to enoxaparin/warfarin for the incidence of recurrent venous thromboembolism (VTE)* or VTE-related death in 5400 patients with objectively confirmed, symptomatic proximal DVT/PE. 2693 patients were randomized to ELIQUIS 10 mg orally twice daily for 7 days followed by 5 mg orally twice daily for 6 months, and 2707 patients were randomized to standard of care, which was initial enoxaparin 1 mg/kg twice daily subcutaneously for at least 5 days (until INR ≥2), followed by warfarin (target INR range: 2.0-3.0) orally for 6 months. The primary efficacy endpoint was recurrent VTE* or VTE-related death, and the primary safety endpoint was major bleeding.

≈90% of patients in the AMPLIFY trial had an unprovoked DVT/PE at baseline.[1]

- The 10% of patients with a provoked DVT/PE were required to have an additional ongoing risk factor in order to be randomized†

*Recurrent symptomatic VTE (nonfatal DVT or nonfatal PE).
†Risk factors included previous episode of DVT/PE, immobilization, history of cancer, active cancer, and known prothrombotic genotype.

To learn more about ELIQUIS, visit **hcp.eliquis.com**

IMPORTANT SAFETY INFORMATION (CONT'D)

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Bleeding Risk:** ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
  - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs.
  - Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.
  - The anticoagulant effect of apixaban can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). An agent to reverse the anti-factor Xa activity of apixaban is available. Please visit www.andexxa.com for more information on availability of a reversal agent.
- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

  The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

  Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.
- **Prosthetic Heart Valves:** The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.
- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.
- **Patients with Antiphospholipid Syndrome (APS):** Direct-acting oral anticoagulants (DOACs) including ELIQUIS are not recommended for patients with a history of thrombosis who are diagnosed with APS. The efficacy and safety of ELIQUIS in patients with APS have not been established.

ADVERSE REACTIONS

- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

- **Combined P-gp and Strong CYP3A4 Inhibitors:** Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

  Clarithromycin
  Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

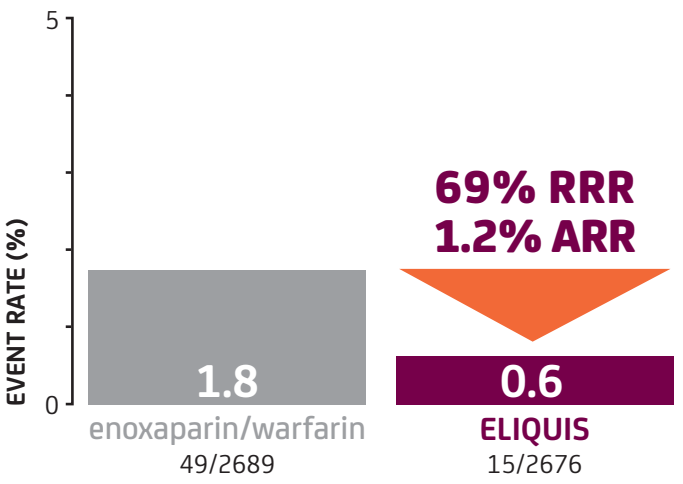
FOR THE TREATMENT OF DVT/PE

Only ELIQUIS demonstrated BOTH superiority in major bleeding events AND comparable efficacy vs enoxaparin/warfarin[1]

SUPERIOR

Major Bleeding‡

RR=0.31 (95% CI: 0.17–0.55); *P*<0.0001

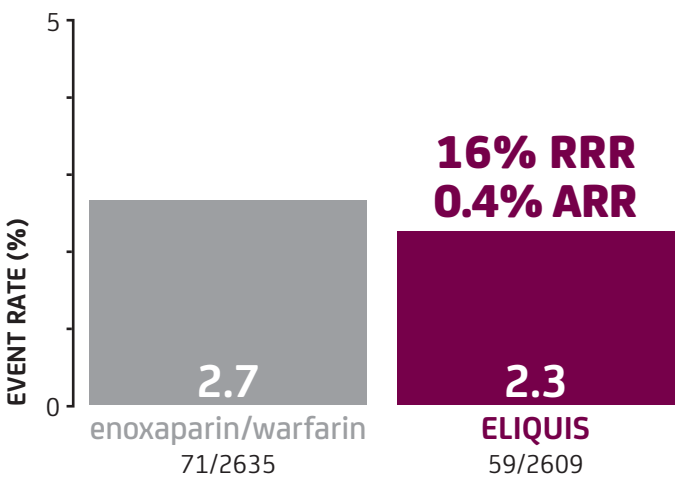


PRIMARY SAFETY ENDPOINT

COMPARABLE

in VTE*/VTE-related death

RR=0.84 (95% CI: 0.60–1.18); *P*<0.0001 for noninferiority



PRIMARY EFFICACY ENDPOINT

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding[1]

- Discontinuation rate due to bleeding events: 0.7% in ELIQUIS-treated patients vs 1.7% with enoxaparin/warfarin[1]
- In AMPLIFY, the most commonly observed adverse reactions in ELIQUIS-treated patients (incidence ≥1%) were epistaxis, contusion, hematuria, menorrhagia, hematoma, hemoptysis, rectal hemorrhage, and gingival bleeding[1]

Major bleeding was defined as clinically overt bleeding accompanied by at least one of the following[2,3]:

1) A decrease in hemoglobin of ≥2 g/dL; 2) A transfusion of 2 or more units of packed red blood cells; 3) Bleeding that occurred in at least 1 of the following critical sites: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, or retroperitoneal; 4) Fatal bleeding

ARR=absolute risk reduction; CI=confidence interval; HR=hazard ratio; INR=international normalized ratio; RR=relative risk; RRR=relative risk reduction.
‡Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS (cont'd)

- **Combined P-gp and Strong CYP3A4 Inducers:** Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.
- **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY

- The limited available data on ELIQUIS use in pregnant women are insufficient to inform drug-associated risks of major birth defects, miscarriage, or adverse developmental outcomes.

Treatment may increase the risk of bleeding during pregnancy and delivery, and in the fetus and neonate.

  – *Labor or delivery*: ELIQUIS use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Consider use of a shorter acting anticoagulant as delivery approaches.

LACTATION

- Breastfeeding is not recommended during treatment with ELIQUIS.

References: 1. Eliquis [package insert]. Bristol-Myers Squibb Company, Princeton, NJ, and Pfizer Inc, New York, NY. **2.** Agnelli G, Buller HR, Cohen A, et al; for AMPLIFY Investigators. Oral apixaban for the treatment of acute venous thromboembolism. *N Engl J Med*. 2013;369(9):799-808. Supplement available at http://www.nejm.org/doi/suppl/10.1056/NEJMoa1302507/suppl_file/nejmoa1302507_appendix.pdf. Accessed December 5, 2018. **3.** Agnelli G, Buller HR, Cohen A, et al. Apixaban for extended treatment of venous thromboembolism. *N Engl J Med*. 2013;368(8):699-708. Supplement available at http://www.nejm.org/doi/suppl/10.1056/NEJMoa1207541/suppl_file/nejmoa 1207541_appendix.pdf. Accessed December 18, 2018.

Please see Brief Summary of Full Prescribing Information, including **Boxed WARNINGS,** on adjacent pages.

Eliquis® (apixaban) tablets 5mg 2.5mg

Bristol-Myers Squibb Pfizer

ELIQUIS® (apixaban) tablets, for oral use

℞ ONLY

Brief Summary of Prescribing Information. For complete prescribing information consult official package insert.

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

(B) SPINAL/EPIDURAL HEMATOMA

(A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration, Warnings and Precautions, and Clinical Studies (14.1) in full Prescribing Information]*.

(B) SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**
- **optimal timing between the administration of ELIQUIS and neuraxial procedures is not known**

[see Warnings and Precautions]

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary *[see Warnings and Precautions]*.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated *[see Warnings and Precautions]*.

INDICATIONS AND USAGE

Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation— ELIQUIS® (apixaban) is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery— ELIQUIS is indicated for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery.

Treatment of Deep Vein Thrombosis—ELIQUIS is indicated for the treatment of DVT.

Treatment of Pulmonary Embolism—ELIQUIS is indicated for the treatment of PE.

Reduction in the Risk of Recurrence of DVT and PE—ELIQUIS is indicated to reduce the risk of recurrent DVT and PE following initial therapy.

DOSAGE AND ADMINISTRATION (Selected information)

Temporary Interruption for Surgery and Other Interventions

ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding *[see Warnings and Precautions]*. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be non-critical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established. (For complete *Dosage and Administration* section, see full Prescribing Information.)

CONTRAINDICATIONS

ELIQUIS is contraindicated in patients with the following conditions:

- Active pathological bleeding *[see Warnings and Precautions and Adverse Reactions]*
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions) *[see Adverse Reactions]*

WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation

Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration (2.4) and Clinical Studies (14.1) in full Prescribing Information]*.

Bleeding

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding *[see Dosage and Administration (2.1) in full Prescribing Information and Adverse Reactions]*.

Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs) *[see Drug Interactions]*.

Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.

Reversal of Anticoagulant Effect

An agent to reverse the anti-factor Xa activity of apixaban is available. The pharmacodynamic effect of ELIQUIS can be expected to persist for at least 24 hours after the last dose, i.e., for about two drug half-lives. Prothrombin complex concentrate (PCC), activated prothrombin complex concentrate or recombinant factor VIIa may be considered, but have not been evaluated in clinical studies *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. When PCCs are used, monitoring for the anticoagulation effect of apixaban using a clotting test (PT, INR, or aPTT) or anti-factor Xa (FXa) activity is not useful and is not recommended. Activated oral charcoal reduces absorption of apixaban, thereby lowering apixaban plasma concentration *[see Overdosage]*.

Hemodialysis does not appear to have a substantial impact on apixaban exposure *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of apixaban. There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving apixaban. There is no experience with systemic hemostatics (desmopressin and aprotinin) in individuals receiving apixaban, and they are not expected to be effective as a reversal agent.

Spinal/Epidural Anesthesia or Puncture

When neuraxial anesthesia (spinal/epidural anesthesia) or spinal/epidural puncture is employed, patients treated with antithrombotic agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently for signs and symptoms of neurological impairment (e.g., numbness or weakness of the legs, or bowel or bladder dysfunction). If neurological compromise is noted, urgent diagnosis and treatment is necessary. Prior to neuraxial intervention the physician should consider the potential benefit versus the risk in anticoagulated patients or in patients to be anticoagulated for thromboprophylaxis.

Patients with Prosthetic Heart Valves

The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves. Therefore, use of ELIQUIS is not recommended in these patients.

Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy

Initiation of ELIQUIS (apixaban) is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

Patients with Antiphospholipid Syndrome

Direct-acting oral anticoagulants (DOACs) including ELIQUIS are not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome (APS). In particular for patients that are triple positive (positive for lupus anticoagulant, anticardiolipin, and anti–beta 2-glycoprotein I antibodies), treatment with DOACs could be associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy. The efficacy and safety of ELIQUIS in patients with APS have not been established.

ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the prescribing information.

- Increased risk of thrombotic events after premature discontinuation *[see Warnings and Precautions]*
- Bleeding *[see Warnings and Precautions]*
- Spinal/epidural anesthesia or puncture *[see Warnings and Precautions]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The safety of ELIQUIS was evaluated in the ARISTOTLE and AVERROES studies *[see Clinical Studies (14) in full Prescribing Information]*, including 11,284 patients exposed to ELIQUIS 5 mg twice daily and 602 patients exposed to ELIQUIS 2.5 mg twice daily. The duration of ELIQUIS exposure was ≥12 months for 9375 patients and ≥24 months for 3369 patients in the two studies. In ARISTOTLE, the mean duration of exposure was 89 weeks (>15,000 patient-years). In AVERROES, the mean duration of exposure was approximately 59 weeks (>3000 patient-years).

The most common reason for treatment discontinuation in both studies was for bleeding-related adverse reactions; in ARISTOTLE this occurred in 1.7% and 2.5% of patients treated with ELIQUIS and warfarin, respectively, and in AVERROES, in 1.5% and 1.3% on ELIQUIS and aspirin, respectively.

Bleeding in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE and AVERROES

Tables 1 and 2 show the number of patients experiencing major bleeding during the treatment period and the bleeding rate (percentage of subjects with at least one bleeding event per 100 patient-years) in ARISTOTLE and AVERROES.

Table 1: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in ARISTOTLE*

	ELIQUIS N=9088 n (per 100 pt-year)	Warfarin N=9052 n (per 100 pt-year)	Hazard Ratio (95% CI)	P-value
Major†	327 (2.13)	462 (3.09)	0.69 (0.60, 0.80)	<0.0001
Intracranial (ICH)‡	52 (0.33)	125 (0.82)	0.41 (0.30, 0.57)	-
Hemorrhagic stroke§	38 (0.24)	74 (0.49)	0.51 (0.34, 0.75)	-
Other ICH	15 (0.10)	51 (0.34)	0.29 (0.16, 0.51)	-
Gastrointestinal (GI)¶	128 (0.83)	141 (0.93)	0.89 (0.70, 1.14)	-
Fatal**	10 (0.06)	37 (0.24)	0.27 (0.13, 0.53)	-
Intracranial	4 (0.03)	30 (0.20)	0.13 (0.05, 0.37)	-
Non-intracranial	6 (0.04)	7 (0.05)	0.84 (0.28, 2.15)	-

* Bleeding events within each subcategory were counted once per subject, but subjects may have contributed events to multiple endpoints. Bleeding events were counted during treatment or within 2 days of stopping study treatment (on-treatment period).
† Defined as clinically overt bleeding accompanied by one or more of the following: a decrease in hemoglobin of ≥2 g/dL, a transfusion of 2 or more units of packed red blood cells, bleeding at a critical site: intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal or with fatal outcome.
‡ Intracranial bleed includes intracerebral, intraventricular, subdural, and subarachnoid bleeding. Any type of hemorrhagic stroke was adjudicated and counted as an intracranial major bleed.
§ On-treatment analysis based on the safety population, compared to ITT analysis presented in Section 14 in the full Prescribing Information.
¶ GI bleed includes upper GI, lower GI, and rectal bleeding.
** Fatal bleeding is an adjudicated death with the primary cause of death as intracranial bleeding or non-intracranial bleeding during the on-treatment period.

In ARISTOTLE, the results for major bleeding were generally consistent across most major subgroups including age, weight, $CHADS_2$ score (a scale from 0 to 6 used to estimate risk of stroke, with higher scores predicting greater risk), prior warfarin use, geographic region, and aspirin use at randomization (Figure 1). Subjects treated with apixaban with diabetes bled more (3.0% per year) than did subjects without diabetes (1.9% per year).

Table 2: Bleeding Events in Patients with Nonvalvular Atrial Fibrillation in AVERROES

	ELIQUIS (apixaban) N=2798 n (%/year)	Aspirin N=2780 n (%/year)	Hazard Ratio (95% CI)	P-value
Major	45 (1.41)	29 (0.92)	1.54 (0.96, 2.45)	0.07
Fatal	5 (0.16)	5 (0.16)	0.99 (0.23, 4.29)	-
Intracranial	11 (0.34)	11 (0.35)	0.99 (0.39, 2.51)	-

Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Other Adverse Reactions

Hypersensitivity reactions (including drug hypersensitivity, such as skin rash, and anaphylactic reactions, such as allergic edema) and syncope were reported in <1% of patients receiving ELIQUIS.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery

The safety of ELIQUIS has been evaluated in 1 Phase II and 3 Phase III studies including 5924 patients exposed to ELIQUIS 2.5 mg twice daily undergoing major orthopedic surgery of the lower limbs (elective hip replacement or elective knee replacement) treated for up to 38 days.

In total, 11% of the patients treated with ELIQUIS 2.5 mg twice daily experienced adverse reactions.

Bleeding results during the treatment period in the Phase III studies are shown in Table 3. Bleeding was assessed in each study beginning with the first dose of double-blind study drug.

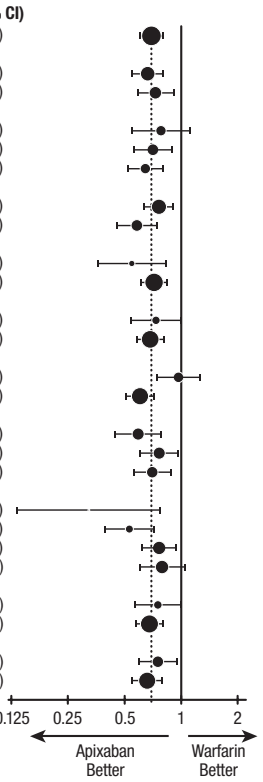
Table 3: Bleeding During the Treatment Period in Patients Undergoing Elective Hip or Knee Replacement Surgery

Bleeding Endpoint*	ADVANCE-3 Hip Replacement Surgery		ADVANCE-2 Knee Replacement Surgery		ADVANCE-1 Knee Replacement Surgery	
	ELIQUIS 2.5 mg po bid 35±3 days	Enoxaparin 40 mg sc qd 35±3 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 40 mg sc qd 12±2 days	ELIQUIS 2.5 mg po bid 12±2 days	Enoxaparin 30 mg sc q12h 12±2 days
	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 9 to 15 hours prior to surgery	First dose 12 to 24 hours post surgery	First dose 12 to 24 hours post surgery
All treated	N=2673	N=2659	N=1501	N=1508	N=1596	N=1588
Major (including surgical site)	22 (0.82%)†	18 (0.68%)	9 (0.60%)‡	14 (0.93%)	11 (0.69%)	22 (1.39%)
Fatal	0	0	0	0	0	1 (0.06%)
Hgb decrease ≥2 g/dL	13 (0.49%)	10 (0.38%)	8 (0.53%)	9 (0.60%)	10 (0.63%)	16 (1.01%)
Transfusion of ≥2 units RBC	16 (0.60%)	14 (0.53%)	5 (0.33%)	9 (0.60%)	9 (0.56%)	18 (1.13%)
Bleed at critical site§	1 (0.04%)	1 (0.04%)	1 (0.07%)	2 (0.13%)	1 (0.06%)	4 (0.25%)
Major + CRNM¶	129 (4.83%)	134 (5.04%)	53 (3.53%)	72 (4.77%)	46 (2.88%)	68 (4.28%)
All	313 (11.71%)	334 (12.56%)	104 (6.93%)	126 (8.36%)	85 (5.33%)	108 (6.80%)

* All bleeding criteria included surgical site bleeding.
† Includes 13 subjects with major bleeding events that occurred before the first dose of apixaban (administered 12 to 24 hours post-surgery).
‡ Includes 5 subjects with major bleeding events that occurred before the first dose of apixaban (administered 12 to 24 hours post-surgery).
§ Intracranial, intraspinal, intraocular, pericardial, an operated joint requiring re-operation or intervention, intramuscular with compartment syndrome, or retroperitoneal. Bleeding into an operated joint requiring re-operation or intervention was present in all patients with this category of bleeding. Events and event rates include one enoxaparin-treated patient in ADVANCE-1 who also had intracranial hemorrhage.
¶ CRNM = clinically relevant nonmajor.

Figure 1: Major Bleeding Hazard Ratios by Baseline Characteristics – ARISTOTLE Study

Subgroup	n of Events / N of Patients (% per year) Apixaban	Warfarin	Hazard Ratio (95% CI)
All Patients	327 / 9088 (2.1)	462 / 9052 (3.1)	0.69 (0.60, 0.80)
Prior Warfarin/VKA Status			
Experienced (57%)	185 / 5196 (2.1)	274 / 5180 (3.2)	0.66 (0.55, 0.80)
Naive (43%)	142 / 3892 (2.2)	188 / 3872 (3.0)	0.73 (0.59, 0.91)
Age			
<65 (30%)	56 / 2723 (1.2)	72 / 2732 (1.5)	0.78 (0.55, 1.11)
≥65 and <75 (39%)	120 / 3529 (2.0)	166 / 3501 (2.8)	0.71 (0.56, 0.89)
≥75 (31%)	151 / 2836 (3.3)	224 / 2819 (5.2)	0.64 (0.52, 0.79)
Sex			
Male (65%)	225 / 5868 (2.3)	294 / 5879 (3.0)	0.76 (0.64, 0.90)
Female (35%)	102 / 3220 (1.9)	168 / 3173 (3.3)	0.58 (0.45, 0.74)
Weight			
≤60 kg (11%)	36 / 1013 (2.3)	62 / 965 (4.3)	0.55 (0.36, 0.83)
>60 kg (89%)	290 / 8043 (2.1)	398 / 8059 (3.0)	0.72 (0.62, 0.83)
Prior Stroke or TIA			
Yes (19%)	77 / 1687 (2.8)	106 / 1735 (3.9)	0.73 (0.54, 0.98)
No (81%)	250 / 7401 (2.0)	356 / 7317 (2.9)	0.68 (0.58, 0.80)
Diabetes Mellitus			
Yes (25%)	112 / 2276 (3.0)	114 / 2250 (3.1)	0.96 (0.74, 1.25)
No (75%)	215 / 6812 (1.9)	348 / 6802 (3.1)	0.60 (0.51, 0.71)
$CHADS_2$ Score			
≤1 (34%)	76 / 3093 (1.4)	126 / 3076 (2.3)	0.59 (0.44, 0.78)
2 (36%)	125 / 3246 (2.3)	163 / 3246 (3.0)	0.76 (0.60, 0.96)
≥3 (30%)	126 / 2749 (2.9)	173 / 2730 (4.1)	0.70 (0.56, 0.88)
Creatinine Clearance			
<30 mL/min (1%)	7 / 136 (3.7)	19 / 132 (11.9)	0.32 (0.13, 0.78)
30-50 mL/min (15%)	66 / 1357 (3.2)	123 / 1380 (6.0)	0.53 (0.39, 0.71)
>50-80 mL/min (42%)	157 / 3807 (2.5)	199 / 3758 (3.2)	0.76 (0.62, 0.94)
>80 mL/min (41%)	96 / 3750 (1.5)	119 / 3746 (1.8)	0.79 (0.61, 1.04)
Geographic Region			
US (19%)	83 / 1716 (2.8)	109 / 1693 (3.8)	0.75 (0.56, 1.00)
Non-US (81%)	244 / 7372 (2.0)	353 / 7359 (2.9)	0.68 (0.57, 0.80)
Aspirin at Randomization			
Yes (31%)	129 / 2846 (2.7)	164 / 2762 (3.7)	0.75 (0.60, 0.95)
No (69%)	198 / 6242 (1.9)	298 / 6290 (2.8)	0.66 (0.55, 0.79)



Note: The figure above presents effects in various subgroups, all of which are baseline characteristics and all of which were prespecified, if not the groupings. The 95% confidence limits that are shown do not take into account how many comparisons were made, nor do they reflect the effect of a particular factor after adjustment for all other factors. Apparent homogeneity or heterogeneity among groups should not be over-interpreted.

Adverse reactions occurring in ≥1% of patients undergoing hip or knee replacement surgery in the 1 Phase II study and the 3 Phase III studies are listed in Table 4.

Table 4: Adverse Reactions Occurring in ≥1% of Patients in Either Group Undergoing Hip or Knee Replacement Surgery

	ELIQUIS (apixaban), n (%) 2.5 mg po bid N=5924	Enoxaparin, n (%) 40 mg sc qd or 30 mg sc q12h N=5904
Nausea	153 (2.6)	159 (2.7)
Anemia (including postoperative and hemorrhagic anemia, and respective laboratory parameters)	153 (2.6)	178 (3.0)
Contusion	83 (1.4)	115 (1.9)
Hemorrhage (including hematoma, and vaginal and urethral hemorrhage)	67 (1.1)	81 (1.4)
Postprocedural hemorrhage (including postprocedural hematoma, wound hemorrhage, vessel puncture-site hematoma and catheter-site hemorrhage)	54 (0.9)	60 (1.0)
Transaminases increased (including alanine aminotransferase increased and alanine aminotransferase abnormal)	50 (0.8)	71 (1.2)
Aspartate aminotransferase increased	47 (0.8)	69 (1.2)
Gamma-glutamyltransferase increased	38 (0.6)	65 (1.1)

Less common adverse reactions in apixaban-treated patients undergoing hip or knee replacement surgery occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: thrombocytopenia (including platelet count decreases)

Vascular disorders: hypotension (including procedural hypotension)

Respiratory, thoracic, and mediastinal disorders: epistaxis

Gastrointestinal disorders: gastrointestinal hemorrhage (including hematemesis and melena), hematochezia

Hepatobiliary disorders: liver function test abnormal, blood alkaline phosphatase increased, blood bilirubin increased

Renal and urinary disorders: hematuria (including respective laboratory parameters)

Injury, poisoning, and procedural complications: wound secretion, incision-site hemorrhage (including incision-site hematoma), operative hemorrhage

Less common adverse reactions in apixaban-treated patients undergoing hip or knee replacement surgery occurring at a frequency of <0.1%:

Gingival bleeding, hemoptysis, hypersensitivity, muscle hemorrhage, ocular hemorrhage (including conjunctival hemorrhage), rectal hemorrhage

Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT or PE

The safety of ELIQUIS has been evaluated in the AMPLIFY and AMPLIFY-EXT studies, including 2676 patients exposed to ELIQUIS 10 mg twice daily, 3359 patients exposed to ELIQUIS 5 mg twice daily, and 840 patients exposed to ELIQUIS 2.5 mg twice daily.

Common adverse reactions (≥1%) were gingival bleeding, epistaxis, contusion, hematuria, rectal hemorrhage, hematoma, menorrhagia, and hemoptysis.

AMPLIFY Study

The mean duration of exposure to ELIQUIS was 154 days and to enoxaparin/warfarin was 152 days in the AMPLIFY study. Adverse reactions related to bleeding occurred in 417 (15.6%) ELIQUIS-treated patients compared to 661 (24.6%) enoxaparin/warfarin-treated patients. The discontinuation rate due to bleeding events was 0.7% in the ELIQUIS-treated patients compared to 1.7% in enoxaparin/warfarin-treated patients in the AMPLIFY study.

In the AMPLIFY study, ELIQUIS was statistically superior to enoxaparin/warfarin in the primary safety endpoint of major bleeding (relative risk 0.31, 95% CI [0.17, 0.55], P-value <0.0001).

Bleeding results from the AMPLIFY study are summarized in Table 5.

Table 5: Bleeding Results in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)	Relative Risk (95% CI)
Major	15 (0.6)	49 (1.8)	0.31 (0.17, 0.55) p<0.0001
CRNM*	103 (3.9)	215 (8.0)	
Major + CRNM	115 (4.3)	261 (9.7)	
Minor	313 (11.7)	505 (18.8)	
All	402 (15.0)	676 (25.1)	

* CRNM = clinically relevant nonmajor bleeding.
Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY study are listed in Table 6.

Table 6: Adverse Reactions Occurring in ≥1% of Patients Treated for DVT and PE in the AMPLIFY Study

	ELIQUIS N=2676 n (%)	Enoxaparin/Warfarin N=2689 n (%)
Epistaxis	77 (2.9)	146 (5.4)
Contusion	49 (1.8)	97 (3.6)
Hematuria	46 (1.7)	102 (3.8)
Menorrhagia	38 (1.4)	30 (1.1)
Hematoma	35 (1.3)	76 (2.8)
Hemoptysis	32 (1.2)	31 (1.2)
Rectal hemorrhage	26 (1.0)	39 (1.5)
Gingival bleeding	26 (1.0)	50 (1.9)

AMPLIFY-EXT Study

The mean duration of exposure to ELIQUIS was approximately 330 days and to placebo was 312 days in the AMPLIFY-EXT study. Adverse reactions related to bleeding occurred in 219 (13.3%) ELIQUIS-treated patients compared to 72 (8.7%) placebo-treated patients. The discontinuation rate due to bleeding events was approximately 1% in the ELIQUIS-treated patients compared to 0.4% in those patients in the placebo group in the AMPLIFY-EXT study.

Bleeding results from the AMPLIFY-EXT study are summarized in Table 7.

Table 7: Bleeding Results in the AMPLIFY-EXT Study

	ELIQUIS 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Major	2 (0.2)	1 (0.1)	4 (0.5)
CRNM*	25 (3.0)	34 (4.2)	19 (2.3)
Major + CRNM	27 (3.2)	35 (4.3)	22 (2.7)
Minor	75 (8.9)	98 (12.1)	58 (7.0)
All	94 (11.2)	121 (14.9)	74 (9.0)

* CRNM = clinically relevant nonmajor bleeding.
Events associated with each endpoint were counted once per subject, but subjects may have contributed events to multiple endpoints.

Adverse reactions occurring in ≥1% of patients in the AMPLIFY-EXT study are listed in Table 8.

Table 8: Adverse Reactions Occurring in ≥1% of Patients Undergoing Extended Treatment for DVT and PE in the AMPLIFY-EXT Study

	ELIQUIS (apixaban) 2.5 mg bid N=840 n (%)	ELIQUIS 5 mg bid N=811 n (%)	Placebo N=826 n (%)
Epistaxis	13 (1.5)	29 (3.6)	9 (1.1)
Hematuria	12 (1.4)	17 (2.1)	9 (1.1)
Hematoma	13 (1.5)	16 (2.0)	10 (1.2)
Contusion	18 (2.1)	18 (2.2)	18 (2.2)
Gingival bleeding	12 (1.4)	9 (1.1)	3 (0.4)

Other Adverse Reactions

Less common adverse reactions in ELIQUIS-treated patients in the AMPLIFY or AMPLIFY-EXT studies occurring at a frequency of ≥0.1% to <1%:

Blood and lymphatic system disorders: hemorrhagic anemia

Gastrointestinal disorders: hematochezia, hemorrhoidal hemorrhage, gastrointestinal hemorrhage, hematemesis, melena, anal hemorrhage

Injury, poisoning, and procedural complications: wound hemorrhage, postprocedural hemorrhage, traumatic hematoma, periorbital hematoma

Musculoskeletal and connective tissue disorders: muscle hemorrhage

Reproductive system and breast disorders: vaginal hemorrhage, metrorrhagia, menometrorrhagia, genital hemorrhage

Vascular disorders: hemorrhage

Skin and subcutaneous tissue disorders: ecchymosis, skin hemorrhage, petechiae

Eye disorders: conjunctival hemorrhage, retinal hemorrhage, eye hemorrhage

Investigations: blood urine present, occult blood positive, occult blood, red blood cells urine positive

General disorders and administration-site conditions: injection-site hematoma, vessel puncture-site hematoma

DRUG INTERACTIONS

Apixaban is a substrate of both CYP3A4 and P-gp. Inhibitors of CYP3A4 and P-gp increase exposure to apixaban and increase the risk of bleeding. Inducers of CYP3A4 and P-gp decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events.

Combined P-gp and Strong CYP3A4 Inhibitors

For patients receiving ELIQUIS 5 mg or 10 mg twice daily, the dose of ELIQUIS should be decreased by 50% when coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir) *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

For patients receiving ELIQUIS at a dose of 2.5 mg twice daily, avoid coadministration with combined P-gp and strong CYP3A4 inhibitors *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Clarithromycin

Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Combined P-gp and Strong CYP3A4 Inducers

Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Anticoagulants and Antiplatelet Agents

Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding.

APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk, post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo. The rate of ISTH major bleeding was 2.8% per year with apixaban versus 0.6% per year with placebo in patients receiving single antiplatelet therapy and was 5.9% per year with apixaban versus 2.5% per year with placebo in those receiving dual antiplatelet therapy.

In ARISTOTLE, concomitant use of aspirin increased the bleeding risk on ELIQUIS from 1.8% per year to 3.4% per year and concomitant use of aspirin and warfarin increased the bleeding risk from 2.7% per year to 4.6% per year. In this clinical trial, there was limited (2.3%) use of dual antiplatelet therapy with ELIQUIS.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

The limited available data on ELIQUIS use in pregnant women are insufficient to inform drug-associated risks of major birth defects, miscarriage, or adverse developmental outcomes. Treatment may increase the risk of bleeding during pregnancy and delivery. In animal reproduction studies, no adverse developmental effects were seen when apixaban was administered to rats (orally), rabbits (intravenously) and mice (orally) during organogenesis at unbound apixaban exposure levels up to 4, 1 and 19 times, respectively, the human exposure based on area under plasma-concentration time curve (AUC) at the Maximum Recommended Human Dose (MRHD) of 5 mg twice daily.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Pregnancy confers an increased risk of thromboembolism that is higher for women with underlying thromboembolic disease and certain high-risk pregnancy conditions. Published data describe that women with a previous history of venous thrombosis are at high risk for recurrence during pregnancy.

Fetal/Neonatal adverse reactions

Use of anticoagulants, including apixaban, may increase the risk of bleeding in the fetus and neonate.

Labor or delivery

All patients receiving anticoagulants, including pregnant women, are at risk for bleeding. ELIQUIS use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Consider use of a shorter acting anticoagulant as delivery approaches *[see Warnings and Precautions]*.

Data

Animal Data

No developmental toxicities were observed when apixaban was administered during organogenesis to rats (orally), rabbits (intravenously) and mice (orally) at unbound apixaban exposure levels 4, 1, and 19 times, respectively, the human exposures at the MRHD. There was no evidence of fetal bleeding, although conceptus exposure was confirmed in rats and rabbits. Oral administration of apixaban to rat dams from gestation day 6 through lactation day 21 at maternal unbound apixaban exposures ranging from 1.4 to 5 times the human exposures at the MRHD was not associated with reduced maternal mortality or reduced conceptus/neonatal viability, although increased incidences of peri-vaginal bleeding were observed in dams at all doses. There was no evidence of neonatal bleeding.

Lactation

Risk Summary

There are no data on the presence of apixaban or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Apixaban and/or its metabolites were present in the milk of rats (see Data). Because human exposure through milk is unknown, breastfeeding is not recommended during treatment with ELIQUIS (apixaban).

Data

Animal Data

Maximal plasma concentrations were observed after 30 minutes following a single oral administration of a 5 mg dose to lactating rats. Maximal milk concentrations were observed 6 hours after dosing. The milk to plasma AUC (0-24) ratio is 30:1 indicating that apixaban can accumulate in milk. The concentrations of apixaban in animal milk does not necessarily predict the concentration of drug in human milk.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total subjects in the ARISTOTLE and AVERROES clinical studies, >69% were 65 years of age and older, and >31% were 75 years of age and older. In the ADVANCE-1, ADVANCE-2, and ADVANCE-3 clinical studies, 50% of subjects were 65 years of age and older, while 16% were 75 years of age and older. In the AMPLIFY and AMPLIFY-EXT clinical studies, >32% of subjects were 65 years of age and older and >13% were 75 years of age and older. No clinically significant differences in safety or effectiveness were observed when comparing subjects in different age groups.

Renal Impairment

Reduction of Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation

The recommended dose is 2.5 mg twice daily in patients with at least two of the following characteristics *[see Dosage and Administration (2.1) in full Prescribing Information]*:

- age greater than or equal to 80 years
- body weight less than or equal to 60 kg
- serum creatinine greater than or equal to 1.5 mg/dL

Patients with End-Stage Renal Disease on Dialysis

Clinical efficacy and safety studies with ELIQUIS did not enroll patients with end-stage renal disease (ESRD) on dialysis. In patients with ESRD maintained on intermittent hemodialysis, administration of ELIQUIS at the usually recommended dose *[see Dosage and Administration (2.1) in full Prescribing Information]* will result in concentrations of apixaban and pharmacodynamic activity similar to those observed in the ARISTOTLE study *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ARISTOTLE.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery, and Treatment of DVT and PE and Reduction in the Risk of Recurrence of DVT and PE

No dose adjustment is recommended for patients with renal impairment, including those with ESRD on dialysis *[see Dosage and Administration (2.1) in full Prescribing Information]*. Clinical efficacy and safety studies with ELIQUIS did not enroll patients with ESRD on dialysis or patients with a CrCl <15 mL/min; therefore, dosing recommendations are based on pharmacokinetic and pharmacodynamic (anti-FXa activity) data in subjects with ESRD maintained on dialysis *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Hepatic Impairment

No dose adjustment is required in patients with mild hepatic impairment (Child-Pugh class A). Because patients with moderate hepatic impairment (Child-Pugh class B) may have intrinsic coagulation abnormalities and there is limited clinical experience with ELIQUIS in these patients, dosing recommendations cannot be provided *[see Clinical Pharmacology (12.2) in full Prescribing Information]*. ELIQUIS is not recommended in patients with severe hepatic impairment (Child-Pugh class C) *[see Clinical Pharmacology (12.2) in full Prescribing Information]*.

OVERDOSAGE

Overdose of ELIQUIS increases the risk of bleeding *[see Warnings and Precautions]*.

In controlled clinical trials, orally administered apixaban in healthy subjects at doses up to 50 mg daily for 3 to 7 days (25 mg twice daily for 7 days or 50 mg once daily for 3 days) had no clinically relevant adverse effects.

In healthy subjects, administration of activated charcoal 2 and 6 hours after ingestion of a 20-mg dose of apixaban reduced mean apixaban AUC by 50% and 27%, respectively. Thus, administration of activated charcoal may be useful in the management of apixaban overdose or accidental ingestion. An agent to reverse the anti-factor Xa activity of apixaban is available.

PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Medication Guide).

Advise patients of the following:

- Not to discontinue ELIQUIS without talking to their physician first.
- That it might take longer than usual for bleeding to stop, and they may bruise or bleed more easily when treated with ELIQUIS. Advise patients about how to recognize bleeding or symptoms of hypovolemia and of the urgent need to report any unusual bleeding to their physician.
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- How to take ELIQUIS if they cannot swallow, or require a nasogastric tube *[see Dosage and Administration (2.6) in full Prescribing Information]*.
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NEWS FROM THE COLLEGE

Submit Comments for Opioid, Pneumonia Clinical Policies

The following drafts are open for comments until Feb. 15:

- "Clinical Policy: Critical Issues Related to Opioids in Adult Patients Presenting to the Emergency Department"
- "Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department with Community-Acquired Pneumonia"

Submit your comments at www.acep.org/pneumonia-comments and www.acep.org/opioids-comments.

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Nominate Your Peers for ACEP Leadership Awards

ACEP is accepting nominations for the 2020 ACEP Awards Program, which annually honors members distinguishing themselves for leadership and excellence in emergency medicine. All members are eligible to submit nominations in one or more award categories, but a nomination form must be completed for each nomination submitted. Nominations must be accompanied by current curriculum vitae. Nominations are due March 1. Get more information at www.acep.org/leadership-awards.

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MIPS: Upcoming Changes You Should Know About

Many of you are all too familiar with the Merit-based Incentive Payment System (MIPS), the major quality reporting program for physicians under Medicare. Each year the Centers for Medicare and Medicaid Services (CMS) revises requirements for MIPS, and CMS recently finalized requirements for calendar year 2020. Read our regulatory blog at www.acep.org/regsandeggs to learn more about the changes to MIPS coming in 2020 and to get some helpful tips about the program.

ACEP Leaders Meet with AAFP

ACEP President Bill Jaquis, MD, FACEP, and President-Elect Mark Rosenberg, DO, FACEP, joined ACEP Executive Director Dean Wilkerson for a meeting with the American Academy of Family Physicians (AAFP) in late November 2019. They discussed the role of family physicians serving emergency departments in rural America, the organizations' shared role in addressing the opioid crisis, bridging ED electronic health records with primary care records for true interoperability, and more.

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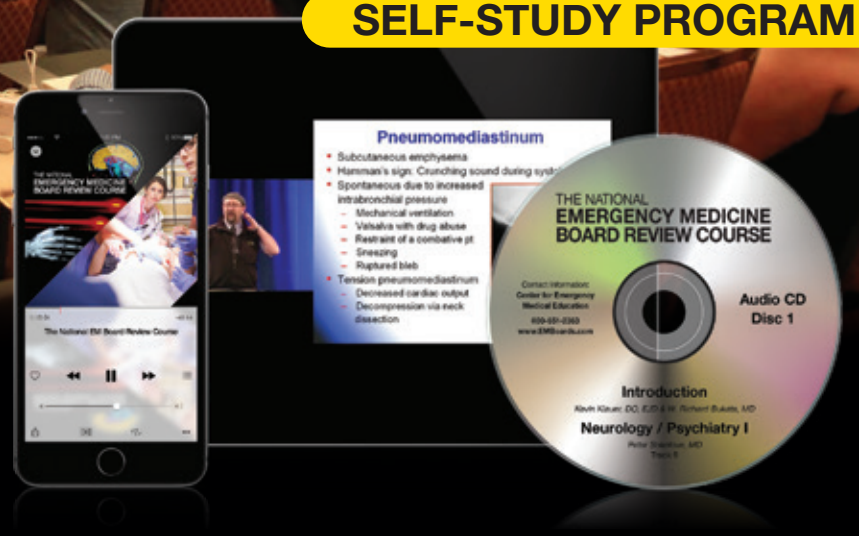

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THE CENTER FOR MEDICAL EDUCATION

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Changing Paths from Academia to Business

Reflections on reinventing oneself and the evolving landscape of emergency care

by JESSE PINES, MD, MBA, MSCE

Have you ever thought about taking your career in an entirely new direction? Maybe you're in the community and you want to get back to academics. For me, it was the opposite. This is my story: why I did it, what I do now, and what I've learned. My hope in sharing is that it might help you think through what matters to you as you look into the future of your own career in medicine.

After 15 years in academic medicine at the University of Pennsylvania in Philadelphia and George Washington University in Washington, D.C., I took a new job at US Acute Care Solutions (USACS) in September 2018 as its national director of clinical innovation. In all honesty, my move was met with both positive and negative feedback. There were many well-wishers (thank you!) but others with pointed questions: Why leave a successful academic career, particularly given the controversial role of management groups like USACS in emergency medicine?

Well, here is why. The first part of my career was dedicated almost entirely to scholarship—primarily writing papers (I love writing) and writing grants (I love less), teaching, and clinical practice. Along the way, I enjoyed success in publishing, great interactions with colleagues, and satisfaction in advancing science in emergency care. I also had opportunities to work in policy circles around Washington, D.C., and in academic leadership.

Like many of you, I follow the Facebook group EM Docs. In many posts I read, I sense undercurrents of angst and burnout. Discussions abound on desires for life redesign, often through reflections on clinical cases or other remarkable work situations.

Sometimes EM Docs posts are disheartening. Many suggest: "This is not what I signed up for!" Yet in reality, that's mostly wrong. We actually knew the pain points. Maybe we just romanticized emergency medicine or didn't fully comprehend its cumulative effects. Perhaps it's not medicine that changes, it's us who change as we grow and age. To no surprise, your 30-year-old self should have different goals than your 50-year-old self, with greater experience in life's successes and failures. Call it what you will—midlife crises or another name—emergency physicians regularly re-examine identity, specifically why we do what we do and to what end.

In the 2018 book, *Designing Your Life: How to Build a Well-Lived, Joyful Life*, authors Bill Burnett and Dave Evans—who also lead the Stanford Life Design Lab—apply design thinking to life and career redesign. The book offers many tools: journaling and self-reflection and a road map for getting "unstuck" through creating and prototyping alternative life plans. The goal of life redesign is to improve job satisfaction and overall happiness across all aspects of life.

Redesigning My Life

As I read this book, nagging questions started haunting me about my career in academics: Can I do this for the next 20 years? If I do, will I have the greatest impact? Am I still growing and learning?

I wasn't so sure. Borrowing from a *Designing Your Life* concept, my work view (ie, why I was working so hard) did not exactly match my life view (ie, what was most worthwhile to me). I had summited my mid-40s, and my pace of learning had slowed. The marginal excitement from the next paper or grant had waned. The reality of complex stakeholders in academics becomes tiresome. I thought to myself: Instead of sitting in an ivory tower writing papers about how to change acute care, maybe I could go and actually try to be a change agent myself. Maybe I could have greater impact in a different role?

My change was not so radical. I did not leave health care or even emergency medicine. I went from one EM community to another, from one platform to another, and from academics to private enterprise (which, in practicality, have similar goals: to provide excellent care at a margin). Instead of just innovating in a single hospital, I am now able to innovate across more than 200 USACS sites and over 6 million ED visits. Much changed, but much stayed the same, like my ability to produce scholarship through the USACS Research Group and my clinical practice.

ILLUSTRATION: SHUTTERSTOCK.COM

So what is my new position? As the USACS national director of clinical innovation, I try to design and implement programs that allow emergency physicians to deliver innovative care, adapt to market changes, remain competitive financially, and operate in novel environments that best leverage our skillset. The goal is to find and implement win-win projects that address age-old struggles in our practice. For example, I am working to implement a system that assesses care experience after discharge and admission with good response rates. This will provide actionable feedback (unlike Press Ganey–like instruments) and allow us to learn more about patients' recovery and follow-up experiences.

Another area of focus is in novel payment models: programs with private and public insurers that align emergency care and population health, allowing us to take financial risk from (and benefit from) good care decisions and value-based care. This includes efforts aimed at lowering rates of CT scan use when clinically unnecessary and lowering hospital admissions. I am also helping to develop new programs in telemedicine, opioids, and direct-to-business models for USACS.

Lessons Learned

Reflecting on my personal career redesign and exposure to the business of emergency care, here are a few lessons:

1. **Midcareer change can create tremendous learning.** Aging can bring complacency without change. Career change disrupts habits and can generate dramatic learning (at least, it did for me), particularly when shouldering new responsibilities. For example, I had to learn the language of business (comparing business and academic physician lingo is not unlike comparing Mandarin and English).
2. **Emergency medicine as we know it is under siege.** This may come as no surprise, but broader forces in medicine and health policy are focused on reducing ED visits and keeping patients away from hospitals (and us). Furthermore, there are great efforts underway to reduce payments to physicians through surprise billing legislation and other policies. In the future, we will probably make either somewhat less or a lot less money for seeing patients. It also means we will increasingly see sicker patients and those with self-pay or public insurance. Sorry if you didn't know that.
3. **Despite this, emergency physicians bring unique value.** When it comes to delivering on value-based care, emergency physicians' abilities to care for the acutely ill and injured patient are unrivaled. In the changing world of new care and payment models, these skills will become increasingly marketable. Don't worry, you will always have a job. But you may have to be nimble regarding how and where you practice.
4. **Real innovation in emergency care is really, really hard.** Trying to implement new approaches is entering a shark pit surrounded by landmines. Even innovations that conceptually make all the sense in the world sometimes get crushed because of competing interests or complacency. Do not discount the powerful effect of personalities, those who create barriers versus those who facilitate.
5. **The success formula to innovation is good idea + alignment + the right team + persistence.** Having a good idea is the easy part. Everyone has good ideas. But you have to have an idea that aligns stakeholder interests and is facilitated by the right people. Show return-on-investment and avoid stomping on someone else's budget. Even getting this recipe right requires persistence because failure is the default and success is the exception.
6. **Business in emergency medicine is not evil.** Feel free to disagree. Great vitriol divides our specialty over how we should organize. Realize that medicine is a business and care cannot be delivered unless there is a business model. In my view, all organizations—large for-profit groups, democratic groups, and nonprofit academic centers—act in their own financial interests within the existing legal framework. I see no angels and no demons. Particularly given lesson 2 above, I find it more fruitful to fight-out than fight-in in emergency medicine.
7. **Re-examine your life, and then redesign and pivot if necessary.** When it comes to your life redesign, take all four aspects into consideration: work, play, love, and health. Take stock of where you are and what alternative realities might look like. Along with *Designing Your Life*, there are a lot of great books out there on the topic. To quote the 1980's hit *Ferris Bueller's Day Off*, "Life moves pretty fast. If you don't stop and look around once in a while, you could miss it."

DR. PINES is the national director of clinical innovation at US Acute Care Solutions and professor of emergency medicine at Drexel University in Philadelphia.

2020 Course Topics

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- Challenges of Managing Pediatric UTIs
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- LPs in Febrile Infants 29-60 Days Old?
- Suicidal Risk: Assessment and Intervention
- Cardiovascular Pearls, 2019
- DKA and Hyperglycemia Update
- Sore Throat: Still Trying to Get It Right
- Sexual / Racial / Ethnic Disparities in the ED
- ACS & PE – ACEP 2019 Guidelines
- Psychiatric Patients: Medical Evaluation
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- Challenges of Atrial Fibrillation - Part 2
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- Sepsis 2019: Hot Off the Press
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- Pearls From *ED Leadership Monthly*
- Urologic Imaging Guidelines
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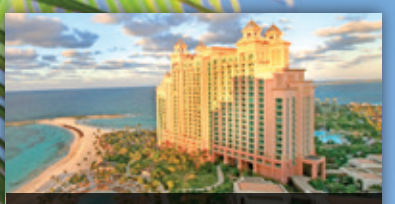

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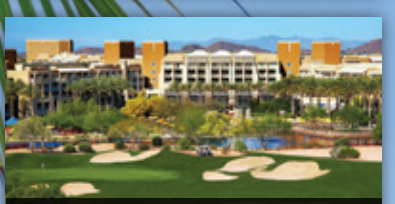

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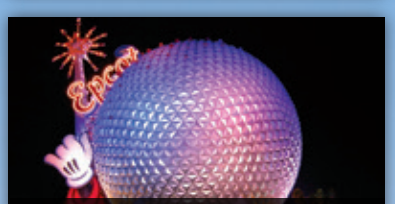

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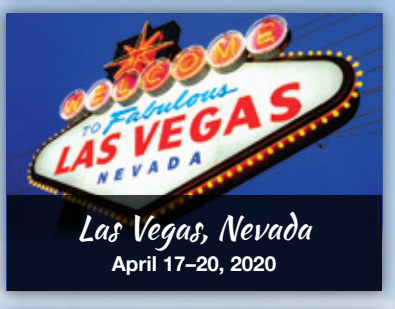

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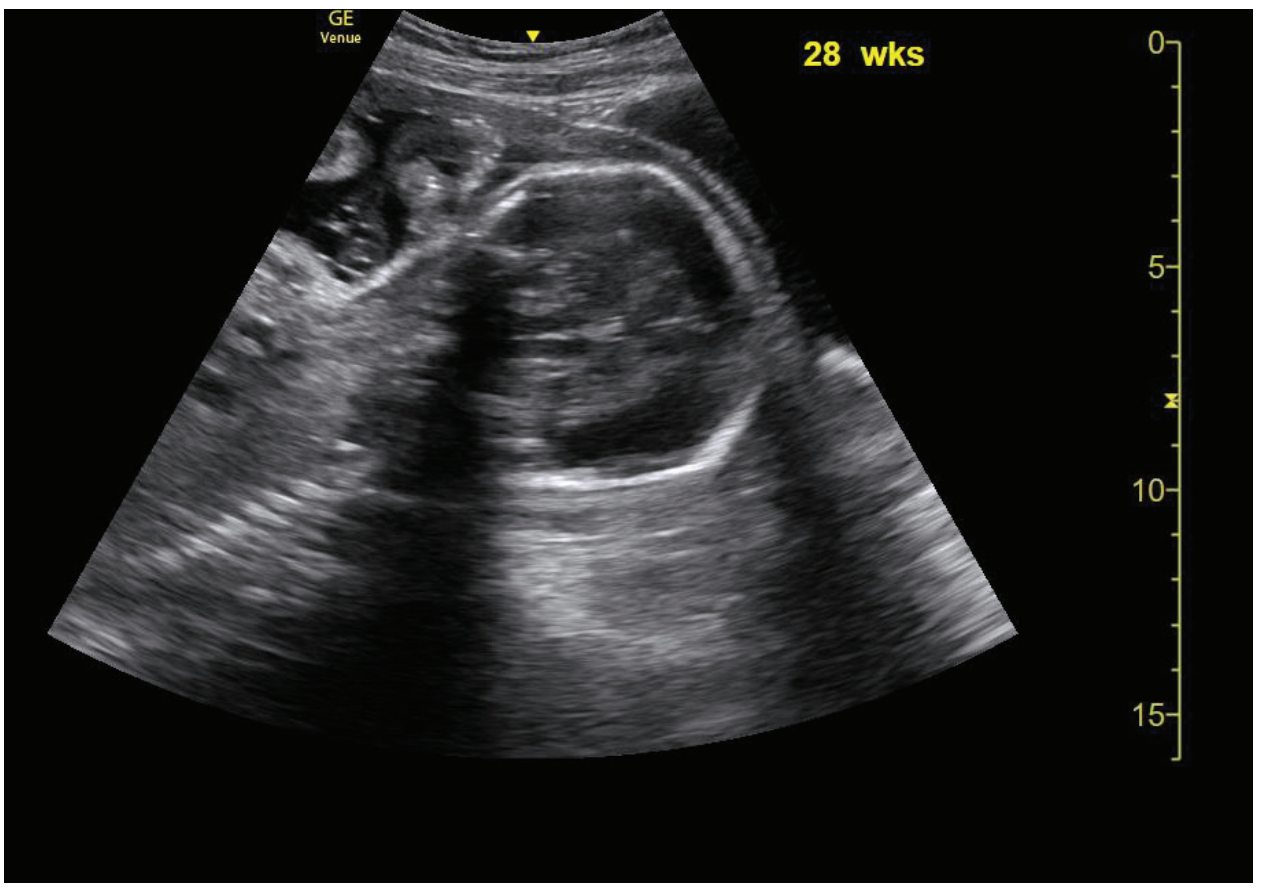
Not So FAST!

Consider the evidence behind trauma ultrasound during pregnancy

by CASEY WILSON, MD; AND LEXUS DICKSON



During your busy shift, you get a call that a 27-year-old G3 P2 female who is 28 weeks pregnant has been involved in a motor vehicle collision. She was the restrained driver in a front-end 25-mile-per-hour collision with airbag deployment. The obstetrician-gynecologist team has tasked you with "clearing" the patient from a trauma perspective before she comes to the labor and delivery floor for monitoring. She complains of some abdominal discomfort. On exam, she has no seatbelt sign. You reach for your trusty ultrasound machine to perform a focused sonography for trauma (FAST) exam and obtain all the necessary views. Then you ask yourself, is the FAST exam even applicable in pregnancy?

Background

Trauma is a leading cause of nonobstetric maternal mortality and affects up to 7 percent of all pregnancies. Both major and minor trauma increase the risk of a pregnancy loss, but pregnant trauma patients are more likely to sustain serious abdominal injuries than nonpregnant trauma patients. The overall fetal loss rate from trauma is reported to be anywhere from 1 percent to 34 percent.[1] The fetal loss rate with penetrating abdominal injuries is far higher, at 73 percent.[2,3] Additionally, life-threatening traumatic injuries to a pregnant patient should always be considered a life-threatening condition for the fetus because maternal death almost always results in fetal death.[4]

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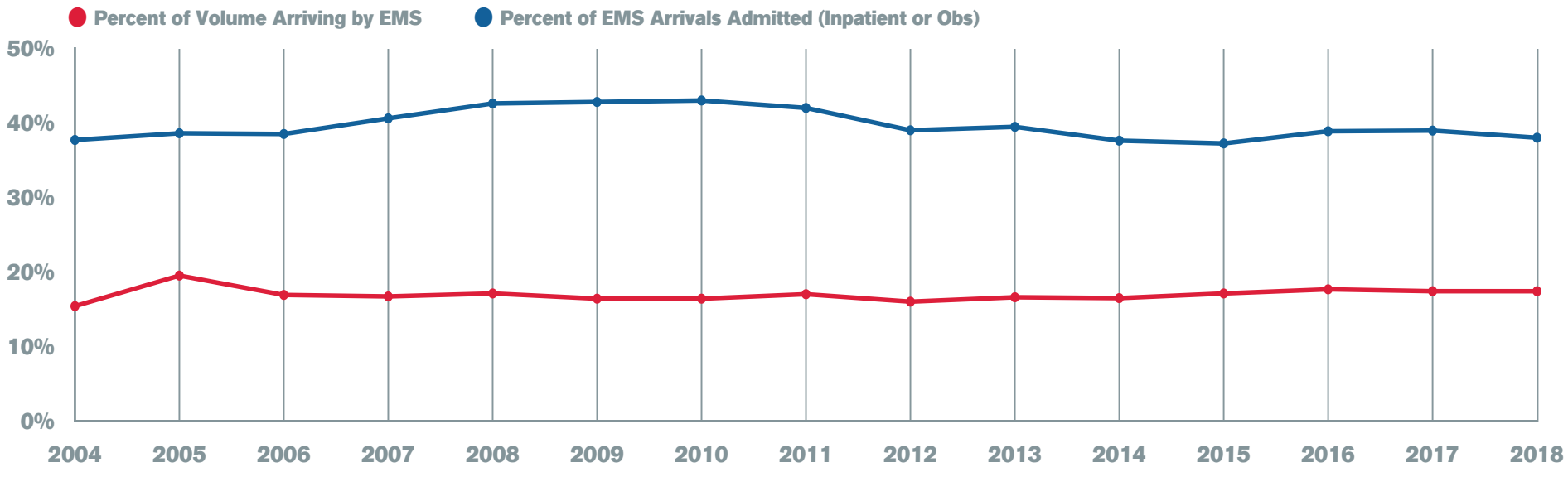


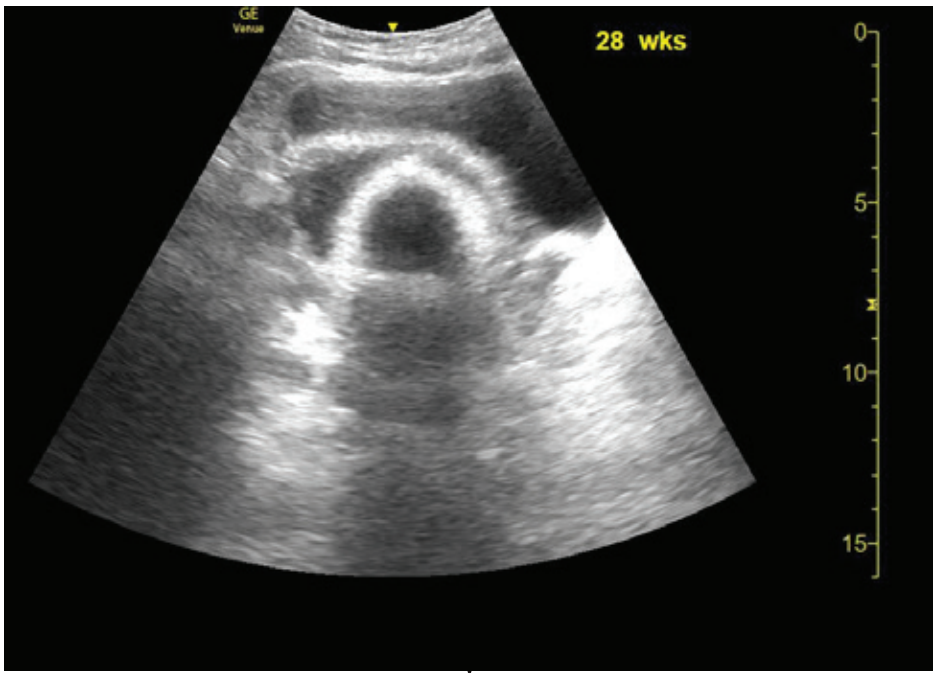
Source: **Emergency Department Benchmarking Alliance (EDBA) Annual ED Survey**

NUMBER of EDs REPORTING
1,910

MEMBERSHIP COMPOSITION

1,782	106	22
GENERAL EDs	PED EDs	SPECIALTY EDs

by **SAM ASHOO, MD, FACEP**, founder and CEO of Admin EM. More at admin-em.com.



Sagittal (opposite page) and transverse (above) pelvic ultrasound of a female who is 28 weeks pregnant.

Because of the risks to both the mother and fetus, emergency and trauma physicians will want to be confident in their physical assessments of pregnant patients with traumatic injuries. Generally, ultrasonography is a preferred imaging modality for this patient population due to lack of radiation exposure. However, the FAST exam, one of the most commonly used assessments to look for free intraperitoneal and pericardial fluid from internal trauma, may be unreliable in pregnant patients.

Limitations of the FAST Exam

The most obvious aspect of the FAST exam that may be different than usual is the pelvic portion of the exam, which can be challenging due to the anatomical changes that accompany pregnancy. Of particular concern is the evaluation of the pouch of Douglas for the presence of hemoperitoneum, which requires special and more advanced ultrasound training than for nonpregnant patients.[5]

The most common cause of pregnancy loss with nonfatal maternal traumatic injury is placental abruption. This is sometimes assessed during the FAST exam, often when attempting to establish ongoing fetal heart motion, fetal activity, amniotic fluid volume, and gestational age.[1,5-7] However, ultrasound is insensitive in diagnosing placental abruption, and a true diagnosis often requires continuous cardiotocographic monitoring.[8,9] Furthermore, as in nonpregnant trauma patients, the FAST exam may fail to identify small amounts of intraperitoneal fluid and specific organ injury in pregnant patients.[10-14]

Sensitivity and Specificity of the FAST Exam

Previous studies on the use of the FAST exam in nonpregnant adult blunt trauma patients have found the FAST exam's detection rate to vary from 79 percent to 98 percent.[15-18] Several studies have attempted to establish the utility of FAST exams as similar in pregnant and nonpregnant women, but the relatively small sample sizes for calculating sensitivity render the findings difficult to rely upon.

When Goodwin and colleagues looked at the use of abdominal ultrasonography to examine pregnant blunt trauma patients, they found a sensitivity of 83 percent (95 percent confidence interval [CI], 36–100 percent) and a specificity of 98 percent (95 percent CI, 93–100 percent). Their sensitivity value determination was based on an evaluation of only six sonographers—although the total sample size was 127 patients.[19]

Brown and colleagues found the sensitivity of screening sonography for use in pregnant patients with blunt abdominal trauma to be 80 percent (95 percent CI, 28–100 percent), but only used five patients to determine this value.[20] Although their reported specificity was 100 percent (95 percent CI, 96–100 percent) for 96 patients without abdominal injury, Brown et al concluded that they "cannot make strong conclusions about sensitivity on the basis of this small study."[20]

In a 10-year retrospective study of ultrasound evaluations in pregnant abdominal trauma patients, Meisinger and colleagues determined the sensitivity and specificity of their institution's extended FAST exam to be 85.7 percent and 99.7 percent, respectively. However, their sensitivity value was calculated based on the findings of only seven patients, and the researchers attributed their higher sensitivity value to the greater training of their sonographers.[21]

A study by Richards and colleagues had the largest number of positive cases (n=23) from which a calculation for sensitivity of the FAST exam could be estimated. They found the sensitivity to be 61 percent, the lowest of all the studies. This low sensitivity compelled them to conclude that the FAST exam "does not rule out intra-abdominal pathology."[22] Their specificity was 94.4 percent for 288 out of 305 patients.[22] Taken together, the sensitivity values in the existing literature, which were calculated based on small sample sizes and have large margins of error, are uncertain indicators of the FAST examination's reliability in detecting signs of blunt trauma within pregnant patients. However, the high specificity in these studies suggests that the presence of positive findings may be enough information to act upon.

Conclusion

The utility of the FAST exam in pregnant trauma patients has yet to be fully validated by existing research and may prove a challenge for providers who are less experienced in ultrasonography. As is the case with many applications of bedside ultrasound, positive findings appear to be quite reliable (ie, high specificities). However, false negatives remain a concern. More research is required to determine the true sensitivity of the FAST exam in this patient subset and to address potential challenges. Researchers continue to emphasize that ultrasound should not be used in place of a diagnostic computed tomographic examination in the treatment of pregnant patients with a high suspicion of internal injury.[5,23-25] Patients (without any further imaging) with concern for occult injury should be admitted to labor and delivery and monitored for 24 hours without adverse events before discharge.

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MS. DICKSON is a medical student at the University of South Carolina.

FACEPs IN THE CROWD

More than 12,000 ACEP members have achieved Fellow status with the College and use the FACEP designation with pride! Here, we highlight ACEP Fellows who have fascinating hobbies and passions outside the emergency department.

NEDRA VINCENT, MD, FACEP

Nedra Vincent, MD, FACEP, has been practicing emergency medicine for 33 years, most recently as an EM physician partner in Mountain View Emergency Physicians Medical Group in Southern California. She fell in love with horses as a young girl and competes at least four times per year in the sport of three-day eventing. Her favorite part is cross country, which involves a miles-long course with 20–30 obstacles to jump. She calls it a "true adrenaline rush," similar to her work in the emergency department. Dr. Vincent is expanding her equine interests by becoming a medical official for an international sport horse event in Southern California and starting to dabble in sport horse breeding. She loves the physicality of riding and says being around horses helps her relax. "Burying my face in a horse's neck is therapeutic."

MARCUS SIMS II, DO, FACEP

Marcus Sims II, DO, FACEP, is a facility medical director for National Medical Professionals in Pearland, Texas. He started flying lessons when he was 13 years old after he and his brother, Chance Sims, DO, a fellow emergency physician, caught the flying bug from their dad. He rekindled his love of flying in August 2018, obtaining his instrument rating in November 2019 and becoming a private pilot in December 2019. Dr. Sims flies Cessna 172s and Piper Arrows and dreams of owning his own plane one day. He said that being an emergency physician is similar to being a pilot in that "both [professions] require you to remain at the top of your game." It's a true family affair for the Sims clan: The brothers love to fly together for quick trips to visit their dad in West Texas, and Dr. Sims takes his four sons flying whenever he can.

EVAN FUSCO, MD, FACEP

Evan Fusco, MD, FACEP, is medical director for Mercy Care Management, based in St. Louis. A longtime Dungeons & Dragons fan who was always fascinated with medieval sword fighting, he started studying historical European martial arts (HEMA) eight years ago. He was drawn to the "cerebral" nature of HEMA, and his group studies a wide range of topics, allowing him to learn aspects of the medieval time period beyond martial arts. "I really like the fact that we're not just bashing one another and playing 'pretend,'" he said. "We are studying, learning, arguing over nuances," which reminds him of the literature debates in emergency medicine. He says both EM and HEMA put you at the edge of your abilities and reveal/punish your missteps in different ways. "This is a break from the ED world for me, a very different type of challenge."

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Chlamydia and Gonorrhea Testing Best Practices

Tips for testing adults and adolescents in the emergency department

by REBECCA BARRON, MD, MPH; STEPHEN LIANG, MD, FACEP; WILLIAM WEBER, MD, MPH; AND ELAINE JOSEPHSON, MD, FACEP

Chlamydia and gonorrhea are the most common and second most common notifiable diseases in the United States, respectively.[1] Rates of both sexually transmitted infections (STIs) have been increasing in recent years.[1] Emergency physicians are on the front lines of diagnosis and treatment of these infections. The ACEP Public Health and Injury Prevention Committee recently issued an information paper on best practices for diagnosing chlamydia and gonorrhea in adult and adolescent patients. Here are highlights from the most current and evidence-based recommendations.

Testing for chlamydia and gonorrhea may be warranted in a range of circumstances, and clinicians should take into consideration patient, provider, and test characteristics when determining how to proceed. Patients with symptoms of infection (whether genital, extragenital, or disseminated), sexual contact with infected individuals, and high-risk demographics may all require testing. Empiric treatment based on clinical suspicion is reasonable when test results are not readily available and/or when follow-up is unlikely. In addition, patients diagnosed with chlamydia or gonorrhea should be offered testing for other STIs, such as syphilis and HIV. Of note, test of cure (ie, attempts to detect therapeutic failure) is generally not necessary.

Historically, microbiological culture was the gold standard for diagnosing chlamydial and gonorrheal infections. This method has been largely replaced by nucleic acid amplification tests (NAATs), which have

CONTINUED *on page 17*

ILLUSTRATION: CHRIS WHISSEN PHOTOS: SHUTTERSTOCK.COM

Now Medical Editor in Chief Jeremy Faust, MD, MS, MA, FACEP, to discuss the role of *JACEP Open* and his vision for this new home for critical emergency medicine research.

JF: What niche does *JACEP Open* fill, and what kind of articles are you looking for?

HW: The goal of *JACEP Open* is to represent the full spectrum of science and knowledge. Submissions from the entire spectrum of science that might be related to emergency medicine research and practicing research are welcome.

JF: That doesn't sound too different from *Annals of Emergency Medicine*. So why a new journal?

HW: It's clear that there is more than enough high-quality material to fill *Annals*, so we really need another venue beside *Annals* to showcase the best of the best. We see *JACEP Open* as a second venue for authors to showcase their best work. We hope that, eventually, the world will see *Annals* and *JACEP Open* as a partnership representing the leading edge of research for our specialty.

JF: When you're starting a brand-new academic journal, how do you convince authors to submit?

HW: One of our highest priorities is to ensure that this is an author-friendly experience. For example, we have great flexibility in the structure of papers. We aim to have a rapid editorial process. For an ideal paper, the peer-review to publication process can be as short as six weeks, and that time frame might be even shorter in the future as we become more adept and streamline our processes.

JF: When authors choose to submit to a journal, prestige is a consideration. How do you attract the best work to a new journal that won't have an impact factor for several years?

HW: Yes, this is a new journal, and it doesn't have an impact factor yet. However, it is backed by ACEP, and it is published by Wiley. Our editorial board is filled with incredibly accomplished and diverse experts from all around the world. And so this is a journal with a lot of credibility from the outset. It's run by a terrific staff with tons of experience and international scientific credibility. Also, the author experience will be enhanced by some of our open access features. We expect to have Medline indexing by the end of 2020. And we expect all articles to be retroactively indexed. Ultimately, we expect an impact factor in 2021.

JF: Other than the fact that *JACEP Open* is free to the readers, what are the other advantages of open access?

HW: Because we are an open access journal, as soon as an accepted paper has completed its production and goes online, it is immediately discoverable by the world. It's immediately discoverable by internet search

CONTINUED *on page 18*

Dr. Wang (left) chats with researchers at ACEP19.

ACEP

CHLAMYDIA AND GONORRHEA TESTING

CONTINUED FROM PAGE 15

sensitivities of up to 100 percent and specificities of 97 percent for diagnosing chlamydia and gonorrhea.[2] For chlamydia testing in women, endocervical and vaginal swabs likely perform equivalently. However, both are superior to urine specimens in terms of sensitivity.[3] Interestingly, self-obtained vaginal swabs perform as well as clinician-obtained swabs and are generally preferred by patients.[4] In men, urine specimens (ideally first-catch) perform at least as well as urethral swabs while maximizing patient comfort.[3-5]

For gonorrhea testing in women, endocervical swabs appear to perform best, while in men, urine specimens are nearly as good as urethral swabs.[6,7] Gram stain from a urethral swab is an option for confirming the diagnosis in symptomatic men but *not* for excluding it.[3] NAATs can be used to evaluate for both chlamydial and gonorrheal extragenital infections, though not all are approved by the U.S. Food and Drug Administration for this purpose. Finally, microbiological culture is still useful in determining antibiotic susceptibility when gonococcal resistance is suspected.

Development of improved point-of-care testing for chlamydia and gonorrhea is underway and has the potential to improve the diagnostic and therapeutic capabilities of emergency physicians in this area.

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DR. BARRON, DR. LIANG, DR. WEBER, and **DR. JOSEPHSON** are members of the ACEP Public Health and Injury Prevention Committee.

engines. And because it is open access material, it floats to the top of open searches like Google. So for authors seeking to have their work easily accessible by the entire world, *JACEP Open* is an excellent forum. Also, unlike other types of publication licenses, in our open access model, the authors actually retain the rights to the work.

JF: How is it going so far in the early months? Are you getting a lot of submissions? How many of those submissions are coming from the *Annals* pathway, and how many are coming as direct submissions?

HW: In our first weeks we've been open for business, there have been nearly 100 submissions, far exceeding our hopes. A portion of the papers are those that had been transferred from the *Annals of Emergency Medicine*, but we have had a large number of papers that have come in directly.

JF: Can you address some of the concerns people have about the system in which authors are paying publication fees? And what about authors who can't afford that?

HW: Open access journals often involve an article publication charge, and *JACEP Open* works along the same model. There are several factors authors should consider when weighing the pros and cons of an article publication charge. First of all, we ensure a quality experience in exchange for this publication charge. We aspire to have articles go through the editorial and production process very quickly and for the article to be widely accessible throughout the entire world on a very rapid basis.

In addition, I think the reality of biomedical publishing is that many journals are charging publication fees now, including some print [non-open access] journals. Some journals are not very open and upfront about their fees. It's not uncommon for an author to work through revisions at a medical journal, have it accepted, and then be surprised by a page charge for their publication. And these are substantial page charges, often totaling well over $1,000. In my view, speaking as a scientist and as an editor, in 10 years it wouldn't surprise me if the vast majority of medical journals move to a model where there's some type of publication charge to authors.

Regarding affordability, there is a waiver system available, and the authors can apply for special consideration in cases of economic hardship. This is rapidly becoming the norm in this space for those who have financial hardships or cannot afford the publication charge.

JF: Something readers may not know about you is that you're an accomplished violinist and orchestral musician. We both share a love of music! I'm wondering whether you think that your background as a violinist makes you a better editor.

HW: Writing a medical paper is exactly like composing a piece of classical music. I work with my students a lot using the same analogies. If you are a classical music fan, you'll recognize that we love classical music because of the beauty of its traditional forms. The sonata form has an introduction, a theme, a second theme and development, and then a repeat of those themes. The reason we love Mozart and Beethoven is partly due to that. There's a beauty in that structure. And I dare say that medical articles very much work the same way. Readers have an expectation that the introduction, methods, results, and discussion will flow in a certain way. For the author, the goal is to have your tune resonate within that framework and to grab the listener's attention. It may sound hokey, but honestly, as an author and as an editor, I'm often listening to what "the piece," (ie, the paper) sounds like a little bit more than actually reading the individual words. All of this explains why two papers perhaps covering the same topic can be so different.

JF: Finally, I think we all want to know how the name *JACEP Open* came about. Can you tell us the history there?

HW: Readers might be fascinated to know that the original name of *Annals of Emergency Medicine* was, in fact, the *Journal of the American College of Emergency Physicians* (*JACEP*). In putting the new journal together and going through a long list of candidate titles, we realized that linkages to the College are extremely important as well as acknowledging our linkage with *Annals of Emergency Medicine*, which is clearly our big brother publication. We homed in on *JACEP Open* as a wonderful way to acknowledge our connections with the College and our partners at *Annals*. At the same time, we are acknowledging that we are using the new open access model and we are a forward-looking journal. So, it's a way to acknowledge our past as well as to look toward the future.

DOING THE MATH TO BENEFIT OUR SPECIALTY

THE EQUITY EQUATION

DR. BLACKSTOCK
is CEO and founder of Advancing Health Equity.

Combat Microaggressions

These "micro" actions can have big impacts, but simple strategies can interrupt them

by UCHÉ BLACKSTOCK, MD

When we encounter overt racism and other forms of discrimination in the workplace, we expect our colleagues of all backgrounds to stand strongly against it. After all, this is the 21st century.

But there is a perception, even among many of our allies, that a relative paucity of open, unconcealed, and uncensored intolerance or prejudice in the workplace means that the effects of these entities are somehow absent. We know that is not the case.

And while people basically know what to do (and what is expected of them) in the face of pure unadulterated bigotry in the workplace, the same can't be said of more subtle digs and jabs, whether intentional or not. These remarks or attacks have a name: microaggressions.

What Is a Microaggression Anyway?

Microaggressions are "brief and commonplace daily verbal, behavioral, and environmental indignities, whether intentional or unintentional, that communicate hostile, derogatory, or negative...slights and insults."[1] The "micro" portion of the expression refers to the perception by the aggressor, not in the hurtful impact this form of aggression can have.

Being on the receiving end of microaggressions in the health care workplace can result in provider burnout and attrition. Often, microaggressions go unrecognized by bystanders because bystanders may not realize something offensive was said, or they just don't know how to respond.

Before delving into what allies can do to help combat microaggressions, it's important to have a more comprehensive understanding of them. There are several subcategories of microaggressions, including microinsults, microinvalidations, and microassaults.[2]

- **Microinsults**, often unconscious, are characterized by behavioral/verbal remarks or comments that convey rudeness and insensitivity and demean a person's heritage or identity.
- **Microinvalidations**, also often unconscious, are verbal comments or behavior that exclude, negate, or nullify the psychological thoughts, feelings, or experiential reality of the targeted person.
- **Microassaults**, more often conscious, are explicit derogations characterized primarily by a violent verbal or nonverbal attack meant to hurt the intended victim through name-calling, avoidant behavior, or purposeful discriminatory actions.

Often when someone hears or experiences a microaggression, they experience an internal dilemma: "Did I interpret that correctly?" or "Did she say what I think she said?" or "Should I say something?" For their part, sometimes well-meaning bystanders who have noticed it are concerned that saying something might only make it worse or that speaking up would add more hurt than it might help.

However, the person directly on the receiving end is likely experiencing a wave of emotions, including humiliation and helplessness. Down the road, these feelings can result in anxiety, depression, sleep difficulties, and diminished confidence. Additionally, racial and gender microaggressions can and do compound, ultimately creating an inhospitable workplace environment that too often leads to attrition.

The power dynamics of the relationships of the players involved also influence how the recipient may feel about responding to the microaggression, both in real time and later. Relationship dynamics can range from colleague-colleague and clinician-patient to supervisor-supervisee. Each situation is unique, with complexities that are difficult to fully understand, thus making their downstream effects more difficult to mitigate.

This is why we need to band together to respond to microaggressions when they happen.

What We Can Do

There are many good reasons to confront a microaggression, both for the offender and the offended. These include helping the offender (who often did not mean to cause harm) realize their bias, changing behavior, and setting a norm that the behavior is neither tolerable nor acceptable.

People tend to judge themselves by their intentions. If they consider themselves to be thoughtful and kind, then the intent of their comment may conflict with its impact and its unintended consequences. When speaking out against a microaggression, we have to be aware that the person being called out can be expected to react in a range of ways, from anger, denial, and minimization to guilty or apology. These are all natural reactions.

That is why one of the bystander strategies for combatting microaggressions is to take action as they occur. Here are some strategies for interrupting and intercepting microaggressions.[3]

- Ask a clarifying question.
- Come from a place of curiosity, then listen actively and openly.
- Tell others about your experience: "I noticed that..."
- Encourage others to consider the impact of their words or actions: "How do you think people feel when..?"
- Own your response. "When I hear your comment, I think/feel..."
- Identify next steps and request appropriate action. "I'd appreciate if you would not..."

For those in supervisory positions, several actions can be taken to help create a workplace environment that minimizes microaggressions. First, set expectations for a safe learning or workplace environment. Second, encourage staff and trainees to speak up when they feel uncomfortable about a situation. Third, if you experience a microaggression, share your story so that others may feel more comfortable sharing their stories. Finally, use of "interrupting microaggression" strategies should be consistently encouraged and modeled to set an example for others in the workplace.

While microaggressions may seem small, they are not. Fortunately, it does not take heroic efforts to stop them from causing immediate and downstream hurt and diminishing the quality of our workplace. However, it takes awareness and willingness to act. Working together, we can prevent the macro effects of microaggressions and decrease their prevalence in the process.

"The Equity Equation" is curated by Dara Kass, MD, and Uché Blackstock, MD.

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PROTECT YOURSELF FROM LEGAL RISK

MEDICOLEGAL MIND

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Discovery and Deposition Primer

Practice and strategy are critical for providing testimony at deposition

by GITA PENSA, MD

PHOTO: SHUTTERSTOCK.COM

"I was going through the depositions and really stressing myself out. Not eating. Not sleeping. And I got pregnant at that time and miscarried shortly after, and obviously causality is difficult to prove, but I always thought that was part of the reason why."

—Interviewee, "Doctors and Litigation: The L Word" podcast

After being served with papers initiating a malpractice lawsuit, the deposition is often the next stress-inducing event in the litigation timeline. Most physicians are unfamiliar with depositions at all, let alone how to perform skillfully during one.

An apt analogy is the EM oral boards: Imagine going into that exam (which is in no way similar to your usual practice environment or written exams) without any knowledge of the structure of the exam or strategies for success. Regardless of your clinical skills, you might fare poorly because of your lack of "boardsmanship." Depositions are similar, and preparation for them—both the practical and psychological aspects—is key to increasing the odds of a favorable outcome in your case.

The Deposition Process

Depositions are just one part of the discovery process, the stage of civil litigation that occurs after the lawsuit is initiated. In certain states, discovery begins only after the plaintiff submits an offer of proof or affidavit of merit, demonstrating that the case has been reviewed by a physician or panel that deems it legitimate. Unfortunately, there is almost always an available "expert" physician willing to craft a theory of negligence in exchange for a tidy sum.

During discovery, parties on both sides gather information to help develop their arguments. Several facets of discovery usually precede depositions, including requests for admissions (getting each side to agree on sets of facts that will not be in dispute during the case), interrogatories (questions each side directs to the other in written form), and requests for production of relevant documents or records. Often, there is intermittent involvement of the court, as each side will inevitably be dissatisfied with the answers or documents produced, which then serves as the impetus for filing motions that compel divulgence of further information. Each motion will be ruled on by the judge after hearing arguments from both sides. Naturally, this takes time; in some cases, the discovery process can last years. While your attorney will be working steadily, your involvement in these steps is less significant, other than answering the interrogatories with your attorney and reviewing any documents your attorney provides.

The deposition is where you first take center stage. A deposition is the sworn testimony of a witness conducted by opposing counsel, often taking place in their office. The plaintiff, defendant(s), additional witnesses, and medical experts hired for their opinion are all deposed separately. Videotaped depositions are less common than simply transcribed ones; you will be notified ahead of time if it will be recorded. Every word will be taken down by a stenographer and turned into a printed book of testimony that can be reviewed, parsed, and subsequently leveraged. Your words will be quoted back to you at trial, sometimes in out-of-context excerpts framed in a way to paint you in the least positive light. This is why it's so important to develop skills in answering questions truthfully, succinctly, and in the words of *your* choosing—not the plaintiff's attorneys. Attorneys have been trained in methods of tricking you into saying things that you don't really mean. Practice, know-how, and boardsmanship—learning those tricks—will keep you in the driver's seat of your own testimony.

Almost as important as your words is your demeanor in a deposition. Both sides—your own attorney and the plaintiff's—will be sizing you up in terms of how you would appear to a jury when under pressure. Are you angry? Do you appear arrogant or callous? Or do you instead appear confident and caring? Regardless of the quality of your care, if it appears you will be unlikeable to a jury, the plaintiff's attorney will do their best to bring you to trial or hold out for a very large settlement. Emotional control is of utmost importance—and easier to achieve if you have been managing your stress.

There are many books about litigation that help demystify depositions and explain with examples how to skillfully answer tough questions. ACEP also has some online preparation tools, including a video with ACEP Past President Greg Henry, MD, FACEP, and a downloadable list of frequently asked questions at deposition—questions that can turn into traps for the unaware—along with examples of how to adeptly handle these challenges.

Here are just a few tips to get you started. (*Note:* this is not exhaustive, and you should defer to your attorney's advice.)

Before Deposition

- Talk to peers and friends. Seek support. It's helpful to talk to someone who has been through it. Self-care is a priority.
- Read a book on malpractice litigation; most have advice on deposition preparation.
- Know the details of your chart well, including all nursing, staff, and EMS notes. You will be given a copy at deposition to reference, but you should already know the details. Anticipate how you will answer tough questions about what was documented.
- Practice answering questions truthfully and succinctly with your attorney, without offering extra information. Speak in specific medical terms; do not try to "teach" the opposing counsel. Do not be demeaning.
- Discuss with your attorney whether to do any research on the relevant medical issues, and keep all research as an "attorney-client work product."
- Discuss how you will handle questions about co-defendants in advance. In general, deposition is not the time for finger-pointing. Do not access or review their records, or you may be deposed about them; review only what your attorney provides you (in which case, you may keep it confidential within attorney-client privilege).

During Deposition

- Pay attention to your attorney. They may object to certain questions and may also give you nonverbal clues when they sense a trap. Physicians have even described their attorneys stepping on their toes under the table!
- Pause and reflect before answering. This helps you focus and gives your attorney an opportunity to object if necessary. Only answer once the question is complete and you know *exactly* what is being asked; ask for clarification if needed. Some examples:
  - » If the attorney asks you run-on questions, ask for them to be broken down.
  - » If the attorney lists data before the question, ask to see the data to confirm it and then clarify the question. Stop looking at the data before you begin to answer.
  - » Be wary of hypothetical or vague questions—they want you to generalize yourself into a corner.
  - » Beware the double-negative question—ask the attorney to rephrase until it's clear, or answer in a full sentence that says exactly what *you* mean.
- Saying you "don't know" or "don't remember" is preferable to vague recollections.
- Do not agree to calling any text or journal article "authoritative."
- Take breaks when you need them. It's usually a long day.
- When the deposition ends, do not talk about it with your attorney until you are well away from the building.

ONE MORE REASON NOT TO ORDER AN X-RAY

SOUND ADVICE

DR. NAGDEV is director of emergency ultrasound at Highland General Hospital, Alameda Health System in Oakland, California.

Ankles and Ultrasound

POCUS can help you evaluate and aspirate

by ARUN NAGDEV, MD

Septic arthritis of the ankle is an uncommon but devastating clinical entity representing 3 percent to 14 percent of all septic arthritis cases.[1] Diagnostics can prove challenging, especially because systemic symptoms like fever and chills are present in fewer than 50 percent of cases. This forces clinicians to rely on nonspecific and often insensitive physical exam findings, such as pain with joint movement and axial loading.

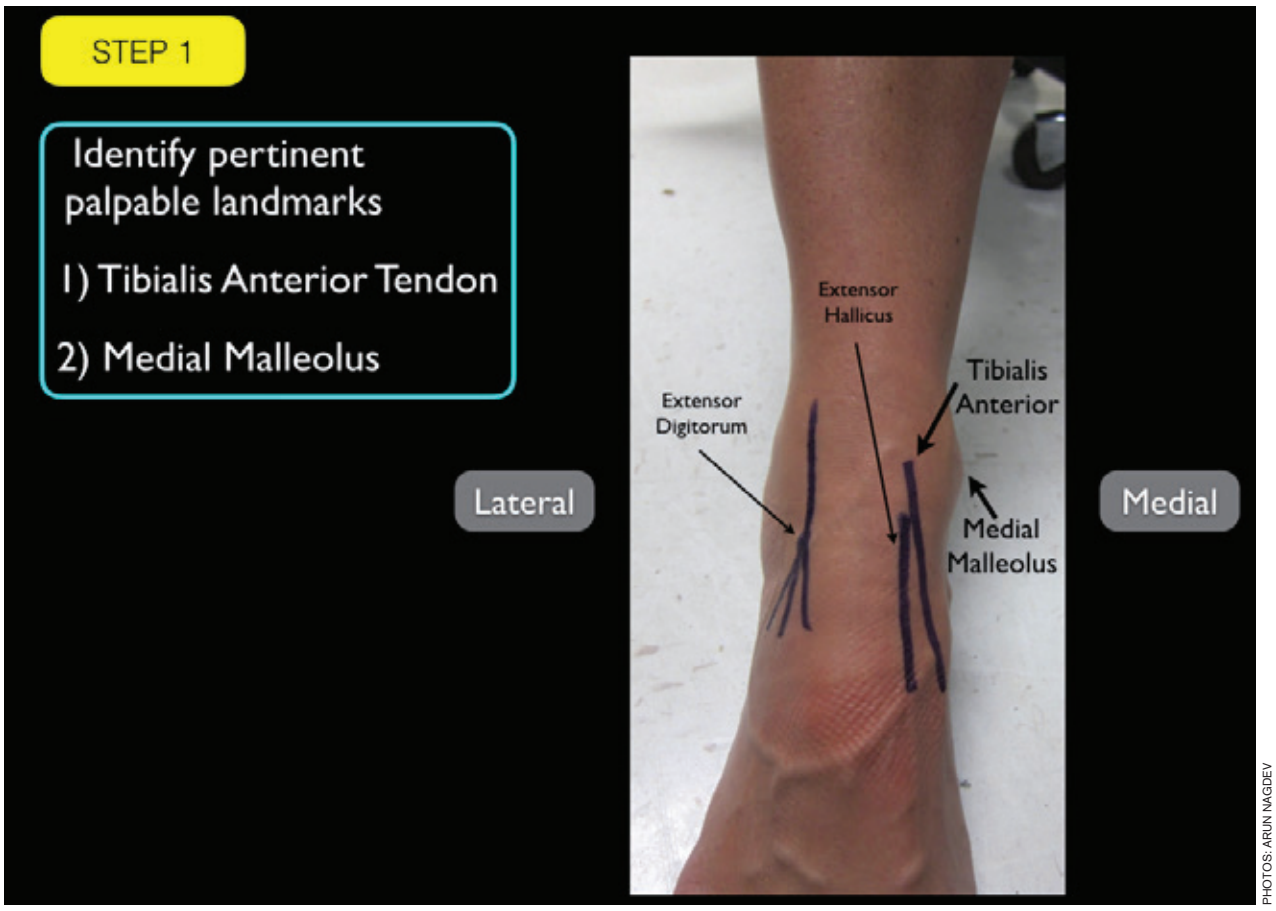
In cases of clinical suspicion of a joint infection, point-of-care ultrasound (POCUS) is an ideal bedside tool to determine the presence of joint capsule effusion. Also, POCUS allows a safe and simplified method for joint aspiration.[1–3]

Ultrasound Examination of the Ankle

Using POCUS for ankle joint assessment starts with good positioning. Place the patient in the supine position with their foot in mild plantar flexion so that the sole rests against the bed. If possible, palpate the anterior tibialis tendon on the anteromedial aspect of the foot. This landmark is easily noted in most patients and acts as an easy starting point when using ultrasound to evaluate the tibiotalar joint.

The goal is to image just under the anterior tibias tendon or just medial to it. The space between the anterior tibias tendon and medial malleolus is free from tendons or arteries, allowing for an unobstructed evaluation of the ankle joint as well as a safe location for aspiration. We recommend using a high-frequency linear transducer because of the shallow depth of the tibiotalar joint (see Step 1).

We also recommend imaging the nonaffected ankle first to determine a true normal. Place the transducer over the distal tibia (with the probe marker oriented caudally) and visualize the bright hyperechoic line of its bony cortex. Slowly slide the transducer toward the ankle until you are over the space between the tibia and talus (see Step 2). A joint capsule effusion will be an anechoic (dark) fluid collection just above the tibiotalar joint and is clearly seen on ultrasound. A superficial cellulitis and/or abscess can be easily differentiated from a deep joint effusion due to its location close to the probe and connection to the overlying skin (see Step 3).



PHOTOS: ARUN NAGDEV

In patients with an obvious effusion of the joint capsule overlying the tibiotalar joint, the clinician can progress to performing the ultrasound-guided aspiration or call a consultant for assistance. Clinical judgment is needed to determine the need for aspiration because other noninfectious entities can produce joint capsule swelling (eg, gout, arthritis, etc.).

Ultrasound-Guided Ankle Arthrocentesis

Joint aspiration is an aseptic procedure (similar to lumbar puncture and central venous access). We recommend covering the transducer with a sterile probe cover. Use the ultrasound to again locate the joint capsule effusion, making sure the ultrasound screen is in your direct line of sight (ie, the system should not be located behind you—your ergonomics and comfort matter). Once the space is located, we recommend placing either a center line or M-mode line to confirm the middle of the transducer is directly over the joint capsule effusion. A skin wheal of 1–2 cc of anesthetic should be placed just adjacent to the medial aspect of the ultrasound transducer (see Step 4). This will be the location for the aspiration needle entry.

Stabilize the ultrasound transducer with your nondominant

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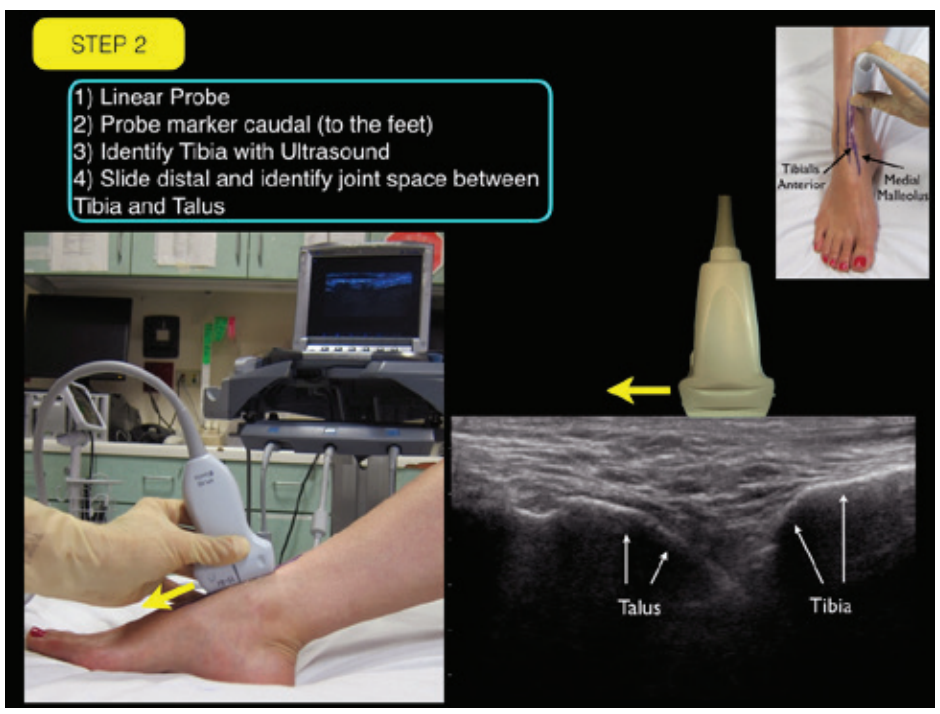

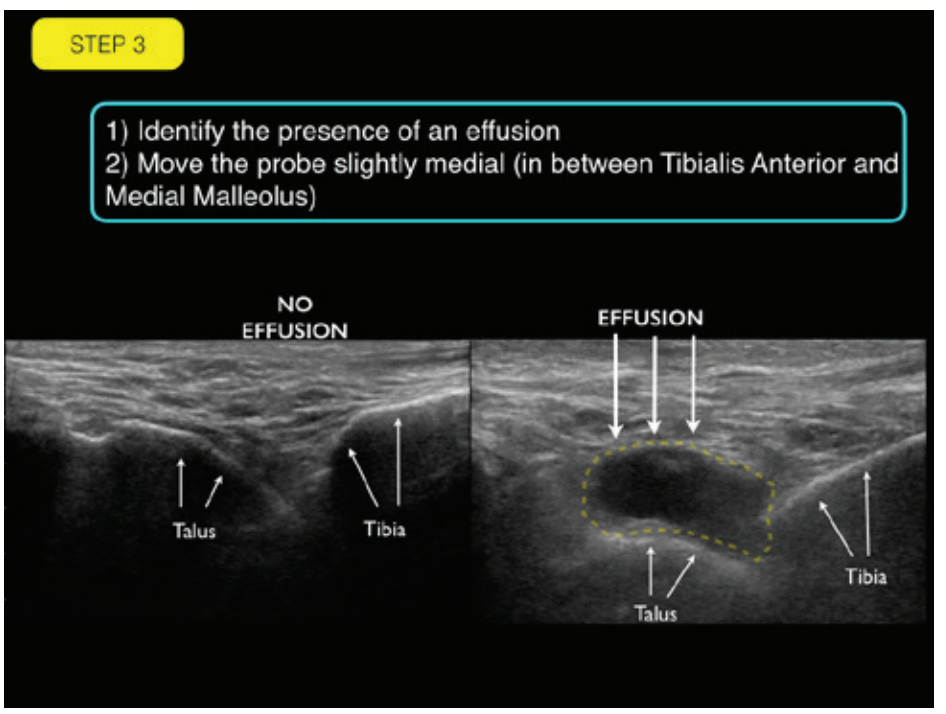

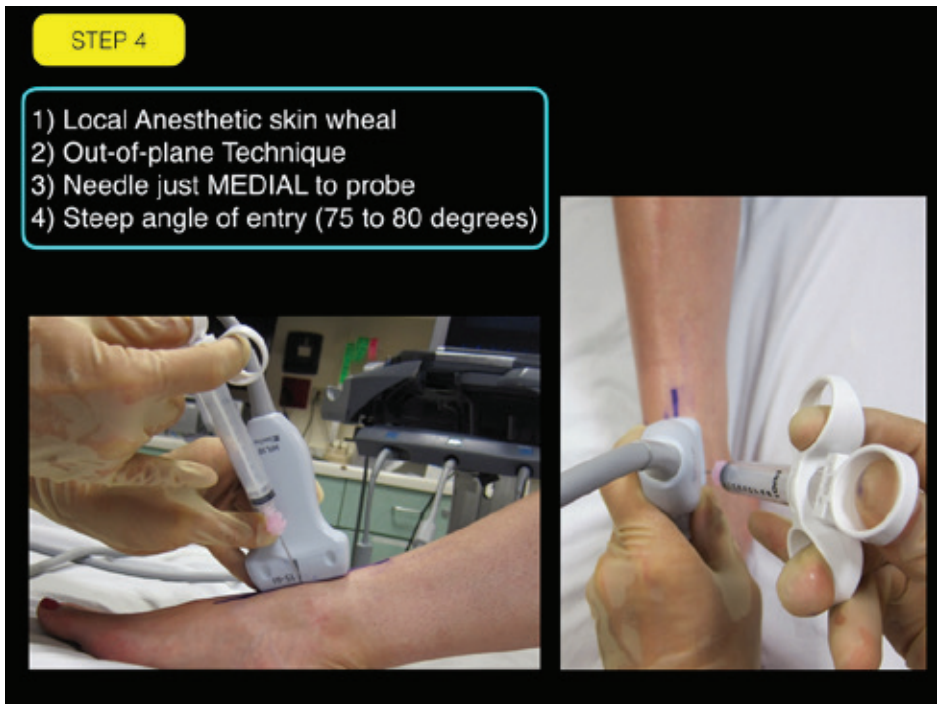

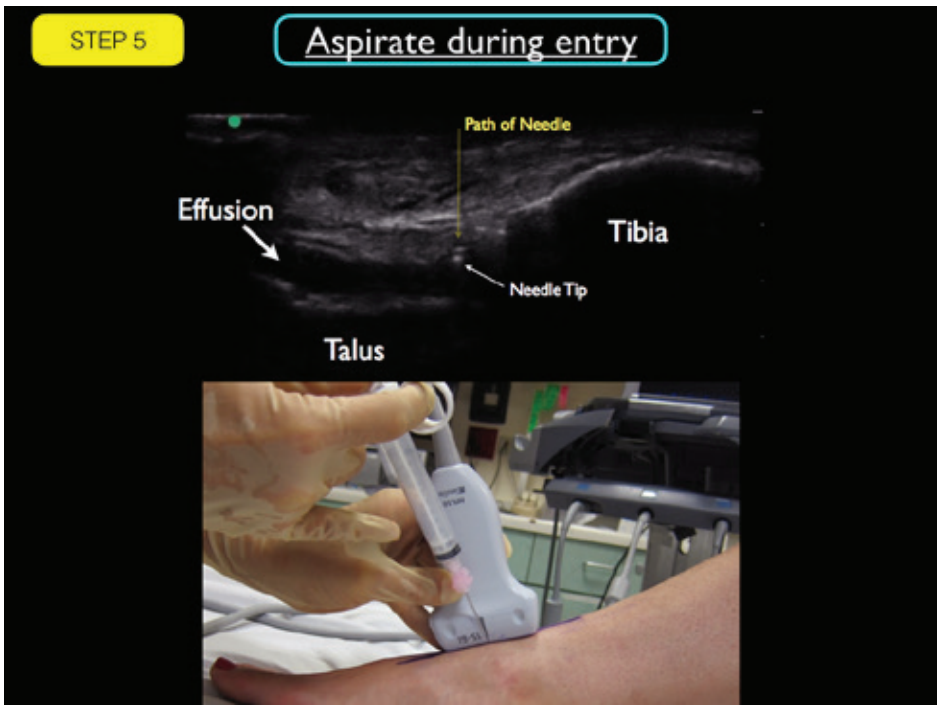

SOUND ADVICE | CONTINUED FROM PAGE 21

hand and have an 18–20-gauge 1.5 in. needle attached to a 5-cc syringe ready for aspiration. Because this is an out-of-plane technique, the operator will not be able visualize the needle entering the joint capsule. However, in our opinion, this is easier overall given the limited space of the tibiotalar joint. Puncture the skin just medial to the midline of the transducer using a very steep angle (just below 90°). The clinician should aspirate as the needle is inserted into the joint capsule because the needle tip may not be clearly visible (see Step 5).

Note: In the photographs for Steps 4 and 5, the sterile cover is *not* placed over the transducer. These images are to demonstrate transducer and needle positioning.

Summary

POCUS evaluation for joint capsule swelling of the ankle can be an important adjunct in the diagnostic evaluation of a patient with a painful and warm lower extremity. A simplified ultrasound technique for visualizing joint capsule swelling of the medial tibiotalar joint can be rapidly performed at bedside. With this critical information, the clinician can more confidently decide whether to perform an ultrasound-guided joint aspiration (or call a consultant for assistance) to determine the presence of a septic joint.

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DOGMA FEELS RIGHT UNTIL YOU STEP IN IT

SKEPTICS' GUIDE TO EMERGENCY MEDICINE

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"Can We Pay You $100 to Not Get a CT?"

A recent study asked the question

by KEN MILNE, MD

The Case

A 24-year-old female enters the emergency department after experiencing a brief loss of consciousness after being hit while playing ice hockey. She feels fine and on evaluation has no complaints of any neurological symptoms, vomiting, or other injury. Her Glasgow Coma Scale score is 15; there is nothing to suggest an open, depressed, or basal skull fracture; and she has no amnesia.

Despite the lack of indication for a computed tomography (CT) scan according to the Canadian CT Head Rule (CCHR), she insists on getting a scan "just to be safe." You'd like to reassure her in an effort to decrease the risks associated with unnecessary testing and to control costs.

Background

The CT scan has become one of the most important diagnostic tests used in the emergency department. It facilitates the rapid identification of several life-threatening conditions. However, there is evidence that it can be overutilized. One specific problem is the overuse of head CTs. A retrospective study demonstrated that more than one-third of head CTs were not indicated based on the CCHR.[1]

One way to decrease unnecessary head CTs is to use clinical decision instruments like the CCHR or the NEXUS Criteria. Despite the validation of these clinical decision tools, adaptation by physicians and acceptance by patients can meet resistance. Many factors influence overtesting, including working in a zero-miss culture. Concern for patient satisfaction scores also can influence decisions to order head CTs that are not clinically indicated.

A new study by Iyengar et al looked at ED patients given a hypothetical low-risk head injury case and assessed the impact a financial incentive as well as varying levels of risk and benefit had on their preference for having a CT scan.[2]

Clinical Question

Can a patient's preference for unnecessary head CT be influenced with financial incentives in conjunction with potential risk and benefit education?

Reference: Iyengar R, Winkels JL, Smith CM, et al. The effect of financial incentives on patient decisions to undergo low-value head computed tomography scans. *Acad Emerg Med*. 2019;26(10):1117-1124.

- **Population:** Adult patients presenting to an academic emergency department.
  - » **Exclusions:** Patients with chest pain, head trauma, altered mental status, or contact precautions; patients treated in the resuscitation bays.
- **Intervention and Comparison:** A hypothetical low-risk head trauma scenario was presented. The clinical scenario suggested against imaging according to the CCHR. Three aspects of the scenario were randomized:
  - » **Benefit:** Presented as either 1 percent or 0.1 percent.
  - » **Risk:** Presented as either 1 percent or 0.1 percent.
  - » **Incentive:** Patients were offered either no money or a $100 financial incentive to forgo the unnecessary CT. Multiple formats were used to present the potential risks and benefits, include percentages (0.1 percent), ratios (1 in 1,000), and visual depictions.
- **Outcome:**
  - » **Primary Outcome:** Percentage of patients who would choose to get a CT scan.
  - » **Secondary Outcome:** Multiple regression analyses to control for potential confounders.

Authors' Conclusions

"Providing financial incentives to forego testing significantly decreased patient preference for testing, even when accounting for test benefit and risk. This work is preliminary, hypothetical, and requires confirmation in larger patient cohorts facing these actual decisions."

Key Results

A total of 913 patients were enrolled. The median age was 45 years, and 56 percent of the population was female. The vast majority of this population identified as Caucasian and had attended at least some college. Overall, 54 percent of patients chose to get a head CT.

The percentage of patients who chose to get a head CT decreased when the education and information provided by the clinicians was paired with the offer of $100. Subjects were also more likely to choose foregoing CT when the reported potential benefit was decreased or when the reported potential risk was increased.

- **Primary Outcome:**
  - » When the potential benefit was reported as 0.1 percent, 49.6 percent of subjects wanted a CT; when the potential benefit was reported as 1 percent, 58.9 percent wanted a CT (odds ratio [OR], 1.48; 95 percent confidence interval [CI,] 1.13–1.92).
  - » When the risk was reported as 0.1 percent, 59.3 percent of people wanted a CT; when the risk was reported as 1 percent, 49.1 percent wanted a CT (OR, 0.66; 95 percent CI, 0.51–0.86).
  - » When no money was offered, 60 percent of people wanted a CT; when $100 was offered to forgo the CT, 48.3 percent of subjects wanted a CT (OR, 0.64; 95 percent CI, 0.49–0.83).
- **Secondary Outcomes:** When adjusted for various potential confounders including age, gender, race, income, level of education, and prior history of health problems, the results remained consistent.

Evidence-Based Medicine Commentary

1. **External validity:** The vast majority of this population was highly educated and Caucasian. There was also a high percentage (24 percent) who worked in health care. This might impact the external validity to other practice populations.
2. **Health literacy:** The authors did a good job explaining the potential risks and benefits of each scenario in multiple ways. However, in the group told the CT would confer a potential benefit of only 0.1 percent, with a 1 percent harm, 50 percent of people still wanted a CT scan. That means even among subjects who were explicitly told their chance of harm was 10 times their chance of benefit, half still wanted a head CT. This may suggest that the patients did not really understand the meanings of these numbers or that the immediate potential benefits described to them were seen as more valuable than delayed potential harms.
3. **Unintended consequences (ie, increases in ED visits for low-risk head injuries):** Would offering cash result in a perverse incentive for a patient to present multiple times to the emergency department with a reported low-risk head injury in the hopes of getting $100 not to get a scan? This would have

CONTINUED *on page 26*

CT, or Not CT

by JOHN G. BOULET, MD

CT, or not CT, that is the question:
Whether 'tis nobler in the brain to suffer
The blows and bumps of trauma wanton,
Or to take meds against a sea of migraines
And by opposing, end them.
To sleep, to die?
No more, no more.
And by a sleep to say we end
The headaches of concussive blows and migraines mighty
That flesh is heir to: 'tis a consummation
Devoutly to be wish'd.
The sleep of migraine, perchance to dream;
To sleep post-trauma, perchance to die?
Therein to dwell upon our end at length ...
For in that sleep of death, what obits there may be:
When we have shuffled off this mortal coil,
Must give us pause, give us pause ...
Calumny, or praise,
Calamity, or eulogy.
For who would bear th'oppressor's wrong, the proud man's contumely,
Th'administrators' scold, the righteous patient's scorn,
Th'intrusive CME and MSO and EMR;
The barristers exclaim: "Delay of care, delay ... of care!"
... of caring?
Oh! For the pangs of dispriz'd medical arts,
Th'insolence and spurns
That doctors suffer of MBAs, every other?
When we ourselves away, our quietus to take?
Would burdens bear
To grunt and sweat, a life so wearing, a work so weary?
Of care, of caring ....
Have we yet no more to give?
No more to give?
But that the dread of something after ... something after ...
Retirement! The second death of self, the second self of death!
Th'undiscovered country, from whose stream
No traveler returns, vexes the will.
And dare we rather hear those headaches "10"
Than fly to the risks of idle time retired, our future selves, of whom we know
... nothing?
Thus does reflection make hesitants of us all,
And duty give order to our days.
And even so, the native hue of resolution Rational,
Is sicklied o'er with the pale cast of second doubts,
Decision trees and algorithms, scoring systems by the score,
Frenetic, frenzied, sleepless nights of battles pitched,
And choices momentous: of death, of life.
This, then, we perceive, reflect, and Science turns awry,
We lose the will ...
To say "no" ....
And CT, after all.

DR. BOULET is a pediatric emergency department attending physician at Huntsville Hospital in Huntsville, Alabama.

By the Numbers

VETERANS & FIREARM INJURY

EVERY DAY

17 veterans die from suicide

VETERANS HAVE

50%

HIGHER risk of suicide than other Americans

33% INCREASE IN VETERAN FIREARM SUICIDE RATE IN THE PAST DECADE

(23% for non-veterans)

THE WEST HAS THE HIGHEST RATE OF VETERAN FIREARM SUICIDES, FOLLOWED CLOSELY BY THE SOUTH

FIREARMS SUICIDE FATALITY RATE

85%

(5% with other methods)

GUN OWNERSHIP INCREASES THE RISK OF SUICIDE 3x

45%

OF VETERANS OWN GUNS

(20% of non-veterans)

IN ONE STUDY, 93% OF VETERANS THINK THE VA SHOULD OFFER VOLUNTARY WAYS FOR AT-RISK VETERANS TO REDUCE THEIR ACCESS TO FIREARMS

Compiled by Andrea Austin and Megan Ranney, MD, MPH, for AFFIRM Research (www.affirmresearch.org). Visit **ACEPNow.com** for the sources of these statistics.

change our behavior, the only thing that matters is whether data on outcomes support us. Here, I will concentrate on the clinically relevant outcome data for various indications and practical aspects comparing IV to oral antibiotics. Once armed with this knowledge, we should feel more comfortable prescribing pills and discharging rather than ordering IVs and admitting.

UTI and Pyelonephritis

Most urinary tract infections (UTIs) can be managed in the outpatient setting. In a Cochrane review of 15 randomized controlled trials (RCTs) comprising 1,743 children and adults with severe UTI, pooled outcomes showed no significant differences between oral and IV antibiotics.[1]

But what about pyelonephritis? In adults with pyelonephritis and complicated UTI, oral fluoroquinolones have been shown to be noninferior to IV antibiotics.[2,3]

And kids? Similarly, a Cochrane review of antibiotics for acute pyelonephritis in well-appearing children older than 1 month of age found no significant differences between oral antibiotics for 14 days and IV antibiotic therapy for three days followed by oral antibiotics, as well as no significant differences in persistent bacteriuria at the end of treatment or persistent kidney damage.[4] A review in *Annals of Emergency Medicine* agreed with this assessment.[5]

Skin and Soft Tissue Infections

In multiple (albeit small) studies, no difference in clinical resolution of cellulitis has been demonstrated between IV and oral antibiotics for simple cellulitis.[6-8] One study, a RCT, found no difference in convenience, complications, effectiveness, overall satisfaction, and mean time to cessation of advancement of cellulitis between oral and IV antibiotics.[8] A Cochrane review of 25 studies including 2,588 patients comparing oral and IV antibiotics for uncomplicated cellulitis looking at "symptoms rated by participant or medical practitioner or proportion symptom-free" found that IV antibiotics were no better than oral ones. In fact, two of the studies suggested that oral antibiotics were more effective![9]

This comports with the Infectious Diseases Society of America recommendation that IV antibiotics for nonpurulent cellulitis be reserved for patients who are immunocompromised or have systemic signs of infection, hemodynamic instability, or altered mental status.[10] In fact, adherence to this guideline has recently been shown to reduce treatment failure rates in ED patients.[11] In a recent retrospective chart review of 500 patients, independent predictors of oral antibiotic treatment failure (defined as hospitalization, change in class of oral antibiotic, or switch to IV therapy after 48 hours of oral therapy) for nonpurulent and soft tissue infections included tachypnea at triage, the presence of chronic ulcers, history of methicillin-resistant *Staphylococcus aureus* colonization or infection, previous recent cellulitis (in the past year), chronic kidney disease, and diabetes.[12]

One reason that IV antibiotics are overused is an incorrect diagnosis of "treatment failure." All too often, patients with skin and soft tissue infections are deemed to have failed oral antibiotics after fewer than 48 hours of oral antibiotics. They then are needlessly switched to IV antibiotics. There is no evidence to support this practice. Treatment failure of simple cellulitis should only be entertained after a 48- to 72-hour trial of oral antibiotics. Even in many of these cases, switching classes of oral antibiotics is sufficient. IV antibiotics are not the automatic answer to "treatment failures."

Community-Acquired Pneumonia

One of the most common reasons for hospital admission is pneumonia. Several RCTs studying treatment approaches in both adults and children with community-acquired pneumonia have been performed. In comparing oral to IV antibiotics, and in assessing the efficacy of early switches from IV to oral antibiotics, there are no data to support the notion of an advantage to IV therapies in most cases.[13-18] A Cochrane review confirms this.[19]

Febrile Neutropenia, Osteomyelitis, and Endocarditis

Let's step it up a bit and consider antibiotic route for cancer patients with febrile neutropenia. Many of us reflexively obtain blood cultures and initiate broad-spectrum antibiotic coverage for these patients without batting an eyelash. And yet again, a Cochrane review of 22 RCTs found that, in patients who were hemodynamically stable without evidence of organ failure or obvious source of infection, oral antibiotics (or an early switch to oral antibiotics) were an acceptable alternative to IV antibiotics.[20] Both the mortality rate and treatment failure rate were similar between groups.

How about osteomyelitis? You guessed it—a Cochrane review of five RCTs found no statistically significant difference in remission rates between oral and IV antibiotics for patients with chronic osteomyelitis, and a recent RCT of more than 1,000 patients with bone or joint infection in *The New England Journal of Medicine* found that the one-year failure rate was similar between patients treated with six weeks of oral antibiotics compared to IV antibiotics of the same duration.[21,22]

Finally, both an RCT from 1996 and a recent one from 2019 found no advantage of oral over IV antibiotics in patients with endocarditis—the former compared oral directly to IV in IV drug users with endocarditis, while the latter compared patients with left-sided endocarditis in stable condition who had been on IV antibiotics for 10 days either continuing IV antibiotics or switching to oral antibiotics.[23,24] All-cause mortality, unplanned cardiac surgery, clinically evident embolism, and relapse of bacteremia were no different between groups.

Bacteremia

Surely, all patients confirmed to have bacte-

remia require at least five days of IV antibiotics! Is nothing sacred? But again, in a recent study of almost 5,000 hospitalized patients with *Enterobacteriaceae* bacteremia, 30-day mortality was no different between patients who received oral step-down after an appropriate clinical response compared with continued IV antibiotics.[25] The authors also found that early transition to oral antibiotics decreased hospital length of stay.

Complications, Efficiency, and Cost

Sometimes patients are admitted to hospital "for IV antibiotics" when they can be safely discharged home on oral antibiotics. The cost savings to the health care system as well as decreased risk of nosocomial infections by avoiding admissions are considerable.[26] There are validated decision tools to help us safely discharge such patients on oral antibiotics for a variety of conditions.[27,28]

Naturally, IV antibiotics are generally more expensive than their oral antibiotic equivalents. However, it isn't only the direct cost of the drugs that needs to be taken into account, but also the indirect costs of using IV antibiotics compared to oral antibiotics. A United Kingdom study looking at nondrug costs of IV antibiotic therapy for patients admitted to hospital with pneumonia or intra-abdominal infections showed that preparation and administration of antibiotics was more time-consuming in those receiving IV antibiotics compared to those receiving oral antibiotics. Use of IV antibiotics was associated with significantly higher workload and additional costs that sometimes were more than the cost of the medications themselves.[29] In the ED, it takes longer to administer IV antibiotics than oral ones. Additionally, there are complications of IV antibiotics to consider, including extravasation injury, phlebitis, as well as local or systemic infection.[30] The risk of bacteraemia *caused* by a peripheral IV can be as high as 0.1%.[26] Even antibiotic-associated diarrhea and secondary infections with *Clostridium difficile* have been shown to be more prevalent in ED patients given a single dose of IV antibiotics before being discharged on oral antibiotics compared to oral antibiotics alone.[31]

Take-Home Message

Taken together, these data support the argument that if we used oral antibiotics for most common infections in the ED, we could safely improve throughput and efficiency and decrease our patients' suffering. So, next time you are faced with a stable non-critically ill patient with a UTI, cellulitis, pneumonia, osteomyelitis, or febrile neutropenia (who is not vomiting and has low aspiration risk), ask yourself whether IV antibiotics are necessary.

If we all chose oral antibiotics most of the time in these situations, we could improve ED efficiency and overcrowding, prevent complications associated with IV insertion, and save our health care system money while safely and effectively providing excellent care for our patients. Meet with your ED group to integrate oral antibiotics choices into your electronic medical records. That alone is likely to help nudge us and our colleagues in the right direction.

Thanks to Dr. Andrew Morris for his contributions to the EM Cases podcasts that inspired this article.

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to be considered.

4. **Health inequities:** There are many examples of health inequities in society. Offering money not to have an unnecessary test may add to this problem. A $100 cash incentive may influence a patient at the lower end of the socioeconomic spectrum compared to a patient at the higher end. Do we really want to reinforce or increase health care gaps based on money rather than the potential benefits and harms of the intervention?
5. **Financial incentive:** Who would pay the $100 financial incentive? Would it come from the hospital? Private or public insurance providers? Would it be deducted from the patient's copayment? (In this study, the cash was intended to be a reduction in one's expected copayment.)
6. **Bottom line:** Money, potential risks, and potential benefits can all influence a patient's behavior in requesting an unnecessary head CT scan.

Case Resolution

You explain to your patient that it is very unlikely she has a serious head injury based on the CCHR. After discussing the risks of a head CT scan and the negligible chance of benefit, she is happy to forgo the scan. Appropriate concussion discharge instructions are provided.

Thank you to Dr. Justin Morgenstern, an emergency physician and the creator of the excellent #FOAMed project called First10EM.com, for his help with this review.

Remember to be skeptical of anything you learn, even if you heard it on the Skeptics' Guide to Emergency Medicine.

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