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*Review*

# Barriers to Antimicrobial Prescribing Changes

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**Abstract**

Antimicrobial resistance remains a global challenge that is not under control. Countries from around the world, including the UK, have developed action plans to counteract this silent pandemic. In the UK, such action plans include antimicrobial stewardship with strategies on early intravenous (IV) to oral antibiotic delivery switch. However, it is evident that despite all this guidance, there are still various barriers or myths preventing the switch. A literature search of studies and other reviews from the past 25 years on the topics of antimicrobial Intravenous-to-Oral Switch (IVOS) was conducted. The literature was reviewed and presented thematically to address perceived myths regarding IVOS. Several studies show that there are various reasons why early IVOS is restricted. Some of these beliefs, or myths, are shared between both the patients and clinicians, such as that IV antimicrobials are superior to the oral options. Some of these barrier beliefs stem from gaps in knowledge about the pharmacology of antibiotics and microbiology, leading to unnecessary IV therapy for resistant organisms. Excessive reliance on inflammatory markers exclusively to measure the severity of an infection is another barrier. Other common myths amongst clinicians are that IV antimicrobials are safer for patients, have no environmental impact, and that they have minimal impact on the clinical team and healthcare organisation. The fear of litigation from the patients for switching early, as well as the hierarchical system for decision making, are other limitations. Although IVOS is not for everyone, it is very evident that there is a lack of awareness about the existing guidance and the risks of not switching when appropriate. All of this is reflected in the beliefs and myths shared by the prescribing clinicians, and more needs to be done to change these views.

**Keywords:** antimicrobial resistance; bioavailability; inflammatory markers; antibiotics; antimicrobial stewardship

## 1. Introduction

Intravenous (IV) medications are prescribed for acutely ill patients on hospital admission for various reasons, including concerns about safe swallowing, inadequate enteral absorption, and the need to quickly achieve effective plasma levels. For many medications, such as analgesics, antihypertensives, or anticonvulsants, switching to oral therapy is often considered routine and straightforward, a perception which may stem from the ease with which the response to therapy can be monitored and reviewed. This is in stark contrast to the situation with antimicrobials, with many studies reporting clinician concern, reluctance, and lack of confidence when reviewing patients for a switch to oral therapy [1,2].

The World Health Organization (WHO) recognised antimicrobial resistance (AMR) as a worldwide threat with the publication of its Global Action Plan in 2014, encouraging regions and countries to act in a coordinated way to halt the development and spread of further resistant antimicrobial strains [3]. In response, the UK published three five-year action plans in 2014, 2019, and 2024 to coordinate a national response to stopping the spread of antimicrobial resistance across human healthcare, veterinary science, farming, and the environment. Published in May 2024 the UK five-year national action plan '*Confronting Antimicrobial Resistance 2024-29*' highlights the role of stewardship in combating the development and spread of antimicrobial resistance and reinforces the importance of timely review following antimicrobial initiation to support rationalisation of therapy including the switching of patients from IV to oral antimicrobial therapy when appropriate [4].

To support decision-making when switching from intravenous antibiotics to oral in infection management, the UK Health Security Agency (UKHSA) produced two initiatives, 'Start Smart then Focus' and the 'Intravenous-to-Oral Switch (IVOS) criteria for prompt switching'. Start Smart then Focus (SSTF), is a toolkit that promotes good practice in the assessment, prescribing, and documentation of infection management [5,6]. It acknowledges the challenges of diagnostic uncertainty in the early phase of infection therapy, which may require empirical broad-spectrum and/or intravenous therapy. However, the SSTF toolkit stresses the importance of an early review of the clinical diagnosis and antimicrobial prescription upon receiving diagnostic and laboratory test results. Patient review should include consideration of the appropriateness of a switch from IV to oral therapy and evaluation of whether antimicrobial therapy is needed at all.

The second initiative, the 'National Antimicrobial Intravenous-to-Oral Switch (IVOS) criteria for prompt

switching' applies to both adults and, more recently, children. These evidence-based decision support aids help identify adults and children by considering patient factors, such as markers for infection and whether the enteral route of administration is feasible to support a switch to oral therapy, as well as infection factors such as type and site of infection that may make continued intravenous administration the preferred therapy. These decision aids are available on the UKHSA website [7].

Even with national IVOS guidance, pathways and resource data suggest that there remains a significant opportunity for appropriate switches of antimicrobial therapy from IV to oral within the acute setting. However, lack of awareness among clinicians of antimicrobial guidelines on IVOS has been demonstrated to be an important barrier [2,8,9].

Prescribers frequently report awareness of the risks of an oral switch to justify continued IV therapy; however, there may be a lack of awareness of the risks of continuing this course of action. This paper will discuss the evidence and address some of the myths encountered when considering a switch in appropriate patients from IV to oral antimicrobials. The article relates to the core elements of specialty training curricula (**Supplementary Material**).

## 2. Myth 1: 'IV Antimicrobials Have Superior Efficacy to Oral Antimicrobials'

Several papers report a belief amongst both physicians and patients that intravenous antibiotics are superior, having better bioavailability and tissue penetration than the oral route and will therefore achieve an earlier cure and prevent re-infection [10,11]. Interestingly, Zhang *et al.* [12] report that this was a belief held by 67% of physician participants.

Numerous oral antibiotics, however, exhibit bioavailability equivalent to or comparable to their parenteral counterparts. Examples of antibiotics with excellent bioavailability of greater than 90% for which IV should rarely be necessitated including clindamycin, doxycycline, levofloxacin, linezolid, metronidazole, and sulfamethoxazole-trimethoprim. Additionally, oral antibiotics with good bioavailability, ranging from 50% to 90% include ampicillin, amoxicillin, and clarithromycin, should be promoted for oral switch after initial dosing in clinically improving patients assessed as being appropriate for switching using the UKHSA tools above [13].

Formulation factors can also be utilised to promote higher levels of antibiotics at the site of infection. Ciprofloxacin has a bioavailability of 70–80%; however, the oral dosage formulation contains 25% more ciprofloxacin than the IV formulation (500 mg oral vs 400 mg IV), thus compensating for the impact of oral bioavailability.

Chemical factors can additionally play a role in the relative partitioning concentration of antimicrobials in different compartments of the body. Although azithromycin and clarithromycin have a bioavailability of approximately 50%, their tissue concentrations are 10–100-fold higher than those in the serum, making them excellent choices when considering an oral switch [14].

There is strong support in the literature for a switch from IV to oral therapy for clinically improving patients for most uncomplicated infections, including community-acquired pneumonia, pyelonephritis, and cellulitis within 24–48 hours of commencing IV therapy [7,15–18]. This evidence shows that IVOS is safe and effective in reducing the length of hospital stay and associated healthcare costs in patients treated for common clinical infection syndromes such as community acquired pneumonia and acute pyelonephritis without compromising the health outcomes.

Even for infections traditionally considered to require IV therapy, substantial evidence demonstrates the efficacy of oral treatment strategies, including for osteomyelitis, endocarditis, and bacteraemia. Tingsgård *et al.* [19] compared the 90-day mortality for individuals with uncomplicated Gram-negative bacteremia who switched to oral antibiotics at four days compared to those who continued IV antibiotics. The results were promising for early transition to oral antibiotics, suggestive of an effective alternative to prolonged IV treatment. Similarly, Hawkins *et al.* [20] examined the use of oral antibiotics for bone and joint infections. They found oral antibiotics to be an effective option, with no increase in the overall duration of antibiotic treatment, reserving IV antibiotics for specific clinical situations. This data further strengthens the evidence provided by the Oral versus Intravenous Antibiotics for Bone and Joint Infection (OVIVA) trial [21] conducted in the UK, which showed non-inferiority of oral antibiotic therapy to intravenous antibiotic therapy when used during the first six weeks of complex orthopaedic infection. Furthermore, the Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis (POET) trial investigated the use of oral antibiotics in stable patients with left-sided infective endocarditis. This study, however, had several limitations and areas of future research to build a strong consensus on the use of oral antibiotics in clinical situations of infective endocarditis based on the type of organisms isolated and the valves involved in the disease progression [22].

## 3. Myth 2: 'My Patient Has a Resistant Organism, Therefore, IV Therapy Is Essential'

A common misconception is that IV antimicrobial therapy must continue until the patient has fully recovered, especially when infections are caused by resistant organisms. This is not always the case, as many oral antibiotics are effective against both community and hospital-acquired resistant infections. For example, oral ciprofloxacin and co-trimoxazole are often used to treat organisms that produce Extended-Spectrum Beta-Lactamases (ESBL) based on susceptibility testing results. Similarly, oral doxycycline, linezolid, and clindamycin, if susceptible, are used to

treat methicillin-resistant *Staphylococcus aureus* (MRSA) infections. Delafloxacin, a relatively new member of the fluoroquinolone class of antimicrobial agents, is active and is available as oral therapy for the treatment of MRSA infections.

Antibiotic failures can and do occur even with extensive IV antibiotic treatments, and many factors contribute to treatment failure, including inadequate source control, host immune response, and comorbidities. Thurber *et al.* [23] compared treatment failures between patients treated exclusively with IV antibiotics and those who transitioned from IV to oral antibiotics for bacteraemia secondary to urinary tract infections. Patients who transitioned from IV to oral antibiotics based on culture-susceptibility data experienced lower rates of treatment failure than those who received exclusive IV therapy [23]. The results of OVIVA trial for Bone and Joint Infections and POET trial for stable endocarditis are promising to show non-inferiority of oral to IV antibiotics [21,22]. The OVIVA trial focused on complex orthopaedic infections during the first 6 weeks, while the POET trial examined partial oral treatment of endocarditis. Both trials demonstrated that oral therapy was as effective as IV therapy in preventing treatment failure, with the added benefits of shorter hospital stays and fewer complications.

## 4. Myth 3: 'The Stewardship Team Will Suggest That All Patients Receiving IV Antibiotic Treatment Be Converted to Oral Therapy Within 72 Hours'

IVOS is not suitable for every patient, and individual patient factors can present rational and acceptable obstacles to oral switch. These factors include gastrointestinal issues such as malabsorption, swallowing dysfunction, and vomiting, as well as situations where adherence is a concern due to altered mental states [2,24]. Besides patient factors, the clinical course of the illness is another significant barrier that often prohibits the switch to oral therapy. These barriers include unstable clinical parameters such as pyrexia, oxygen dependency, and hemodynamic instability, and are captured as justification to continue IV therapy in the UKHSA pathway [2,7].

There are clinical situations when prolonged IV antibiotic treatment is crucial despite potential risks, since the benefits of treatment outweigh these risks. Some of these critical illnesses include *Staphylococcus aureus* bacteraemia, undrainable abscesses, meningitis, brain abscess, and graft infections. Similarly, line-associated infections where long lines need to be salvaged usually require IV antimicrobial treatment.

Timely and relevant microbiological test results, such as blood and urine cultures, are essential for determining whether an oral antibiotic is appropriate and effective for managing an infection. However, these results can only be obtained if appropriate samples are collected promptly, ideally before the initiation of antibiotic therapy.

Delays in obtaining microbiology results can lead to unnecessarily prolonged IV treatment. Relevant microbiological findings are typically expected within 72 hours, underscoring the importance of early diagnostic testing during the initial clinical presentation. When combined with clinical assessment, these results support timely decisions regarding IVOS therapy.

## 5. Myth 4: 'My Patient Needs IV Treatment Until the Inflammatory Markers Have Returned to Normal'

Inflammatory markers, such as C-reactive protein (CRP), white blood cell (WBC) count and erythrocyte sedimentation rate (ESR), have several limitations when used to manage infections, including poor diagnostic accuracy and lack of specificity [25]. The sensitivity of these biochemical markers for bone and joint infections ranges from 52% to 83%, and a normal result does not necessarily rule out infection. These markers are non-specific indicators of inflammation, and elevated levels can be observed in many non-infectious conditions, such as autoimmune diseases, steroid use, and malignancies and therefore should not be used in the diagnosis or monitoring of infection. Another biomarker, procalcitonin (PCT) assay, was approved by the U.S. Food and Drug Administration (FDA) in 2016 for antibiotic stewardship purposes, particularly in the context of sepsis. Its use is not recommended in most of the international (American and British) guidelines on respiratory diseases because of variable and insufficient evidence limiting its clinical utility to complex infections and intensive care settings [26]. Raised PCT levels are seen in various non-infective conditions such as pancreatitis, burns, malignancy and trauma [27]. Consequently, these markers cannot be exclusively relied upon for the diagnosis and monitoring of infections. In conclusion, using only inflammation indicators to decide when to stop intravenous (IV) drug injection is irrational because these markers are not specific to the underlying cause of inflammation, can be elevated by non-infectious conditions, or even paradoxically increased by the drug itself, making clinical assessment of the patient and the specific context crucial for accurate decision-making. Reliance solely on inflammatory markers can lead to incorrect decisions about antibiotic therapy, potentially causing prolonged treatment or the development of drug resistance. Post-antibiotic effects on inflammatory markers are complex, requiring careful monitoring to ensure the infection is truly resolved and that the benefits of normalized markers don't outweigh potential long-term harm.

## 6. Myth 5: 'IV Antimicrobials Have No Patient Risks'

Intravenous therapy requires the insertion of a peripheral venous catheter (PVC); however, half of these

catheters require unplanned removal due to adverse events, which result in patients' harm, such as phlebitis, extravasation, or infection [28]. While infections may be localised, catheter insertion also increases the risk of systemic infections or catheter-related bloodstream infections (CRBSI), which have significant 30-day and 90-day mortality rates of 18.3% and 24.2%, respectively.

The use of intravenous antibiotics carries an increased risk of medication errors from drug preparation to dosing and monitoring of drug levels, as the bioavailability of intravenous antibiotics is high, and the therapeutic dose range is often narrow. This can have serious consequences for patients [29]. An appropriate switch to oral therapy can reduce such complications and improve patient outcomes. In addition to reducing infection and medication errors, switching to oral therapy eliminates the pain or discomfort associated with intravenous catheters and removes the restrictions on mobility and daily activities imposed by intravenous equipment such as infusion pumps, thereby promoting the recovery process and exerting a positive psychological impact.

There are certain intravenous antibiotics that, when administered simultaneously with other drugs that can result in toxicity or drug-drug interactions. For instance, aminoglycosides, when given with loop diuretics such as furosemide, can increase the risk of ototoxicity. Similarly, vancomycin, when administered along with piperacillin-tazobactam, significantly increases the risk of nephrotoxicity, requiring close monitoring of renal function during the therapy. Tigecycline, belonging to a relatively newer class of antibiotics, can have significant drug-drug interactions with immunosuppressant drugs like tacrolimus and ciclosporin that may warrant reduction in the dose, if necessary, with careful monitoring [30].

## 7. Myth 6: 'Being a Nurse Practitioner or Junior Doctor, I Shouldn't Plan IVOS, Particularly Over the Weekend'

Two qualitative studies exploring the reasons and rationale for the failure to implement Intravenous-to-Oral Switch (IVOS) highlighted hierarchy within healthcare as a significant barrier [8,11]. Hamilton *et al.* [8] reported that one-third of nurses do not request an IVOS because they perceive it to be a doctor's responsibility. Whilst Broom *et al.* [11] found that delays often occur in switching to oral therapy because junior staff defer decision-making to senior physicians, who do not always participate in daily ward rounds. A Delphi consensus conducted by Warburton *et al.* [9] with nurses, pharmacists, and doctors identified weekends as an additional organisational barrier. This is primarily due to the lack of treatment reviews over weekends, resulting from limited medical staffing.

Whilst the UKHSA IVOS tool does not overcome the perceived hierarchy, it provides an evidence-based tool to support decision making for all grades and professions of prescribers. In order to have a significant impact on the inappropriate use of IV antibiotics, this hierarchy will somehow need to be addressed.

## 8. Myth 7: 'Patients Will Complain If Switched to Oral Therapy'

Interestingly, Broom *et al.* [11] report that an increasing number of doctors perceive consumerism as a barrier to implementing IVOS. This perception stems from fears of litigation and complaints from patients, who, like consumers, are becoming more demanding and have higher expectations. While there is limited evidence to support or refute the claim that patients specifically demand IV therapy, they report that over 75% of prescriber participants in a National Health Service (NHS) hospital in northeast England recognised consumerism as a barrier to making the switch to oral from IV antimicrobial therapy.

## 9. Myth 8: 'Longer Durations of IV Antibiotics Have No Impact on the Clinical Team or Healthcare Organization'

Most hospitalised patients receive IV antimicrobials at some point during their stay. While the clinical risks and benefits to the individual patient of continuing IV treatment beyond the point when an oral switch is possible have been discussed, extended unnecessary IV therapy also poses additional risks for the healthcare organisation.

Healthcare professionals recognise that the preparation, administration, and disposal of IV medications require considerably more time than oral medications. A 2023 study revealed that each IV medication occupied 22 minutes of nursing time for preparation and administration, while oral medications required only 80 seconds [31]. This substantial difference suggests that switching appropriate patients from, for example, a three-times-a-day IV regimen to oral therapy could free up to one hour of nursing time per patient per day. Conversely, persisting with unnecessary IV therapies engages nursing staff in medication-related tasks, often out of sight of patients and colleagues, and detracts from patient-facing responsibilities.

Data from UK acute hospitals show that, on average, 0.9 doses of IV antibiotics are administered for every occupied bed day [32], whilst NHS England data demonstrates that 15–60% of patients receiving IV antibiotics are suitable for a switch to oral therapy [33]. Translating these figures to a typical 1000-bed hospital would equate to 900 doses of IV antibiotics administered daily, of which at least 10% (or 90 doses) could be easily switched to oral therapy. These unnecessary and easy-to-switch IV doses occupy 30 hours of nursing time each day (Fig. 1).

Beyond the time investment, the financial cost of IV antibiotics tends to be greater than that of oral preparations. This disparity arises not just from the price of the drugs themselves but also from the ancillary items needed for intravenous administration. Moreover, these ancillary items carry additional hidden costs [34]. Their production, trans-

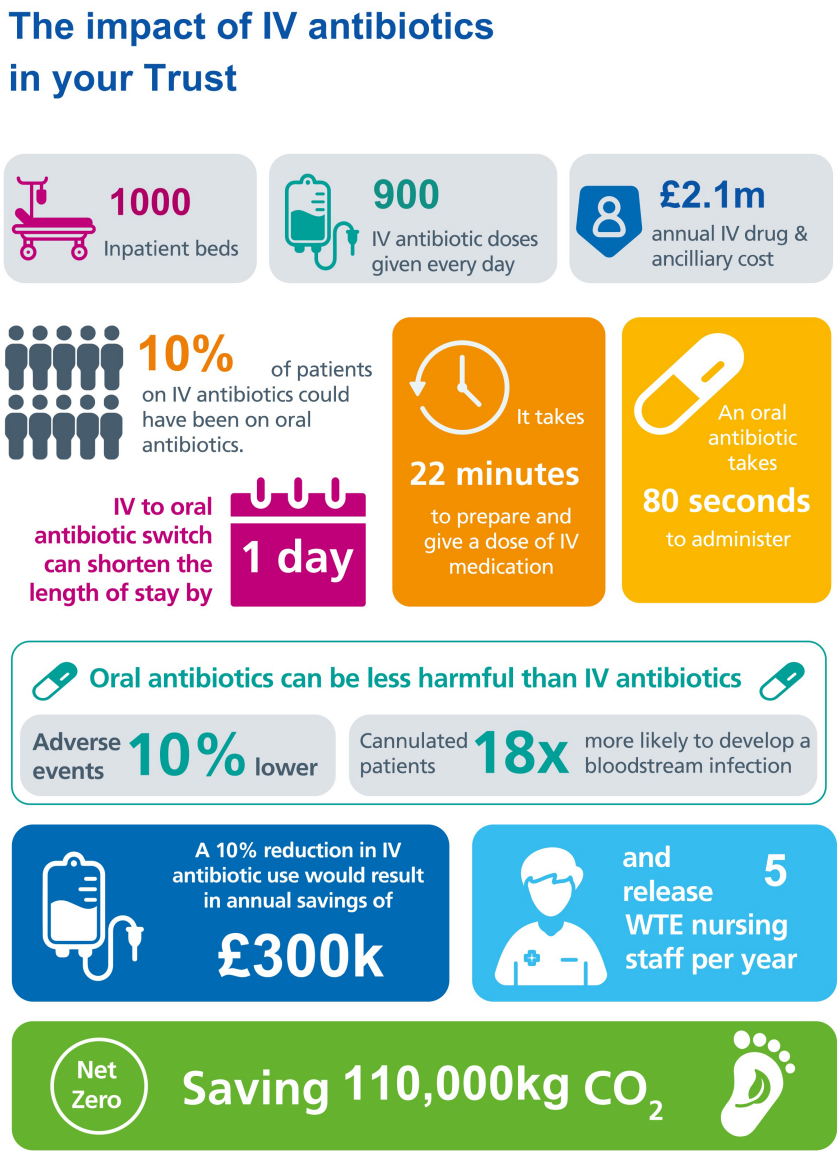


**Fig. 1. Summary of organisational impact of a 1000-bed hospital with a 10% Intravenous-to-Oral Switch (IVOS).** Developed by Abigail Jenkins and Heidi Twaites, University Hospitals Birmingham NHS Foundation Trust, 2024 (Adobe InDesign 19.0.1, Adobe, 2024, San Jose, CA, USA and Adobe Illustrator 28.6, Adobe, 2024, San Jose, CA, USA). IV, intravenous; WTE, Whole Time Equivalents.

portation, and eventual incineration contribute to a significant carbon footprint, highlighting an environmental consideration alongside the financial one. For the typical 1000-bed hospital administering 900 IV antibiotic doses each day, the potential savings from a 10% switch to oral therapy would be over £110,000 per year from just ancillaries alone.

## 10. Myth 9: 'My Prescribing Choices Don't Affect the Environment'

Intravenous medicines have been found to have a 100 times greater impact on carbon emissions compared to their oral equivalents, with 80% of this impact attributable to ancillaries such as giving sets, peripheral venous catheters, and syringes [35,36]. Data from the University of Leeds suggests that in a hypothetical 1000-bed hospital, a 10% reduction in the use of IV antibiotics could reduce carbon dioxide emissions by 65,000 kg per year. An informed shift from intravenous to oral antibiotics can offer substantial benefits in terms of nursing efficiency, as well as broader cost and environmental impacts.

## 11. Conclusion

Antibiotic decisions regarding IVOS are a critical part of antimicrobial stewardship strategy, as early switch can have benefits to patients, healthcare staff, and hospital systems. Patient benefits include reduced risk of IV access-associated adverse effects, increased patient com-

fort, and reduced length of hospital stay, resulting in decreased healthcare costs. IVOS decisions are affected by three main factors that include prescribing behaviours influenced by background antimicrobial stewardship (AMS) knowledge, myths and beliefs, patient factors such as patients' expectations, risks of litigation and complaints, and hierarchical leadership structure in healthcare teams affecting decision-making processes.

IVOS is not for every patient and can carry risks in clinical situations where the benefits of IV treatment outweigh the harms. The myths and gaps in the knowledge should be addressed to enact sustained change in prescribing behaviours. Resources are available within the healthcare systems and at the national level to support changes in prescribing and timely IVOS as a good AMS practice.

## Key Points

- Antimicrobial resistance poses a significant global public health threat, contributing to significant mortality and impacting various aspects of health and the economy.
- Switching patients from intravenous (IV) to oral antibiotic therapy is a crucial aspect of antimicrobial stewardship and should be based on established guidelines or tools and clinical judgment.
- Barriers and myths surrounding the switch from IV to oral antibiotics can hinder early de-escalation, leading to longer hospital stays and potentially increased healthcare costs.
- Some of the barriers include perceived clinical superiority of IV antibiotics, misconceptions about oral bioavailability and patient factors.
- It is crucial to address misconceptions and knowledge gaps among healthcare professionals to improve Intravenous-to-Oral Switches (IVOS), ultimately leading to changes in prescribing behaviours.

## Availability of Data and Materials

Not applicable.

## Author Contributions

AJ suggested and designed the study. UAA, GB, and ACO performed the research. AJ drafted the manuscript. UAA, GB, and ACO revised the literature and analysed the data. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

Not applicable.


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## Conflict of Interest

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## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/BJHM51725.

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