

INTERNAL MEDICINE SOCIETY OF AUSTRALIA AND NEW ZEALAND: TOP 5 LOW-VALUE PRACTICES AND INTERVENTIONS

IMSANZ represents over 700 Consultant Physicians and trainees in Internal Medicine (also known as General Medicine or General and Acute Care Medicine) within Australia and New Zealand. The Society provides a mechanism for developing the academic and professional profile of general medicine and seeks to advocate for and sponsor the educational training, research and workforce requirements of general internal medicine.

1. Avoid medication-related harm in older patients (>65 years) receiving 5 or more regularly used medicines by performing a complete medication review and deprescribing whenever appropriate

Studies show that the risk of medication-related harm rises once the number of regularly prescribed medicines exceeds five; this risk increases exponentially as the number reaches eight or more. Medicines that deserve particular attention are benzodiazepines and other sedative-hypnotics, anti-psychotics, hypoglycaemic agents, antithrombotic agents, anti-hypertensives, and anti-anginal agents.

Trying to achieve aggressive treatment targets, such as BP <130/80 or HbA1c <7 per cent, in frail older patients with multiple co-morbidities confers little benefit and a higher risk of harm.

Discontinuation should be considered where past indications for specific medicines are no longer valid, the risk of harm outweighs the benefits within a patient's remaining life span, or medicines are associated with past toxicity or non-adherence.

Supporting Evidence

- Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol* 2012; 65: 989-95.
- McKean M, Pillans P, Scott IA. A medication review and deprescribing method for hospitalised older patients receiving multiple medications. *Intern Med J* 2016; 46: 35-42.
- Scott IA, Gray LC, Martin JH, Mitchell CA. Effects of a drug minimization guide on prescribing intentions in elderly persons with polypharmacy. *Drugs Aging* 2012; 29: 659-667
- Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy – the process of deprescribing. *JAMA Intern Med* 2015; 175: 827-834.

2. Don't request daily full blood counts, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) as measures of response to antibiotic treatment if patients are clinically improving

The decision on whether or not to cease antibiotic treatment or switch from intravenous (IV) to oral antibiotics should be guided by the results of microbiological cultures indicating bacterial species and antimicrobial sensitivities, and evidence of defervescence and improved clinical status rather than by changes in the levels of white cell count (WCC) from a full blood count, C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR).

However, these markers can help to predict poor prognosis in patients with severe infections in whom the clinical response may be difficult to determine (e.g. immunosuppressed patients or those who are critically ill or those at risk of drug-resistant hospital-acquired infections). In these cases, the failure of markedly elevated CRP and WCC to decrease by specified amounts would suggest that the antimicrobial therapy is not being effective.

While no references could be found that explicitly support not using ESR or CRP in mild to moderate infections, available evidence suggests that their use is only of benefit in severe infections.

Supporting Evidence

- Bruns A, Oosterheert J, Hak E, et al. Usefulness of consecutive C-reactive protein measurements in follow-up of severe community-acquired pneumonia. *Eur Respir J* 2008; 32(3):726-32.
- Coelho L, Póvoa P, Almeida E, et al. Usefulness of C-reactive protein in monitoring the severe community-acquired pneumonia clinical course. *Critical Care*. 2007;11(4):R92.
- Litao M, Kamat D. Erythrocyte sedimentation rate and C-reactive protein: How best to use them in clinical practice. *Pediatr Annals* 2014; 43: 417-420.

3. Once patients have become afebrile (non-feverish) and are clinically improving, don't continue prescribing intravenous antibiotics to those with uncomplicated infections and no high-risk features if they are tolerant of oral antibiotics

Patients with uncomplicated infections not requiring prolonged antibiotic therapy and with no high-risk features should be switched from intravenous (IV) to oral antibiotics once they are afebrile, clinically improving and able to tolerate oral medication. In hospital, this often occurs by day three. Exceptions to this rule are those suffering life threatening or deep-seated infections (such as suspected endocarditis, osteomyelitis or meningitis), and high risk patients (such as immunocompromised patients including from HIV, intravenous drug use, underlying advanced cancer, or documented multi-resistant bacteraemia or hospital-acquired infection).

There is no evidence to support the belief that oral medications are insufficiently bioavailable to be as effective as IV medications, or that the same agent must be used both IV and orally.

The scope for early IV-to-oral conversion has broadened, owing to the advent of newer, more potent oral agents that achieve higher and more consistent serum and tissue concentration. Moreover, earlier switchover from IV-to-oral therapy reduces the risk of cannula-related infections, carries no risk of thrombophlebitis, and allows for earlier discharge and reduced cost.

Supporting Evidence

- Aboltins CA, Hutchinson AF, Sinnappu RN, et al. Oral versus parenteral antimicrobials for the treatment of cellulitis: a randomized non-inferiority trial. *J Antimicrob Chemother*. 2015;70(2):581-6.
- Athanassa Z, Makris G, Dimopoulos G, Falagas ME. Early switch to oral treatment in patients with moderate to severe community-acquired pneumonia: a meta-analysis. *Drugs*. 2008;68(17):2469-81. doi: 10.2165/0003495-200868170-00005.
- Béique L, Zvonar R. Addressing concerns about changing the route of antimicrobial administration from intravenous to oral in adult inpatients. *Can J Hosp Pharm* 2015;68(4):318-26
- Cyriac et al. Switch over from intravenous to oral therapy: A concise overview. *J Pharmacol Pharmacother* 2014;5(2):83-7
- Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010; 50(2):133-64
- Solomkin JS, Reinhart HH, Dellinger EP, et al. Results of a randomized trial comparing sequential intravenous/oral treatment with ciprofloxacin plus metronidazole to imipenem/cilastatin for intra-abdominal infections. The Intra-Abdominal Infection Study Group. *Ann Surg*. 1996;223(3):303-15.

4. Don't request Holter monitoring, carotid duplex scans, echocardiography, electroencephalograms (EEGs) or telemetry in patients with first presentation of uncomplicated syncope and no high risk features

Holter monitoring, carotid duplex scans, echocardiography, electroencephalograms (EEGs) and telemetry have very low diagnostic yield in patients with uncomplicated syncope and no clinical features of, or risk factors for, the following:

- arrhythmia (e.g. palpitations preceding syncope, exertional syncope, unheralded syncope, history suggestive of heart failure or ischaemic heart disease)
- carotid stenosis (syncope would need to be associated with focal neurological symptoms or signs suggestive of transient ischaemic attack),
- cardiac valvular disorders (e.g. definite heart murmurs) or
- seizures (very rarely present as syncope with no other epileptic features e.g. tongue biting, urinary incontinence, post-ictal confusion, muscle pain).

Most syncopal episodes are vasovagal or secondary to postural hypotension for which careful history and lying and standing blood pressure measurements are the most important diagnostic criteria combined with standard 12-lead ECG.

Supporting evidence

- Johnson P, Ammar H, Zohdy W, et al. Yield of diagnostic tests and its impact on cost in adult patients with syncope presenting to a community hospital. *South Med J* 2014; 107(11):707-14.
- Mendu M, McAvay G, Lampert R, et al. Yield of diagnostic tests in evaluating syncopal episodes in older patients. *Arch Intern Med* 2009; 169(14):1299-305.
- Parry SW, Tan MP. An approach to the evaluation and management of syncope in adults. *BMJ* 2010; 340: c880.
- Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS). Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J* 2009; 30(21): 2631-71.

5. Don't request computerised tomography pulmonary angiography (CTPA) as first-choice investigation in non-pregnant adult patients with low risk of pulmonary thromboembolism (PTE) by Wells' score (score <= 4); imaging can be avoided in low risk patients if D-dimer test is negative after adjusting for age

The D-dimer test is highly sensitive for deep vein thrombosis and pulmonary thromboembolism, such that a negative result in non-pregnant adults (adjusted for age) rules out this condition in patients with low pre-test probability. A positive result is however non-specific and may be due to many other conditions apart from PTE. In ruling out PTE, D-dimer assay should be the first choice investigation in patients classified as being low risk according to the Well's score (equal to or less than 4).

These considerations are heightened by the risks associated with CTPA testing such as radiation exposure and incidental imaging findings, e.g. lung nodules and adrenal lesions that may provoke further investigations and diagnosis of isolated small subsegmental emboli whose natural history is unknown and for which anticoagulation is not yet shown to be of benefit. There is however a 1-3% failure rate with a low risk Well's score and negative D-dimer prediction method, so close follow-up is indicated in all patients in whom a D-dimer has been requested. Note that laboratories do not report age adjusted values, though it is well known that D-dimer levels rise with age in the presence of co-morbidities.

An example of age adjustment, endorsed by the clinical guidelines committee of the American College of Physicians (see reference from Raja et al below) quotes an upper limit of normal for D-dimer tests equal to age \times 10 ug/L, rather than a generic upper limit of 500 ug/L. Clinical judgement is necessary in applying this adjustment method, with some reports adopting a more conservative formulae of age \times 5 ug/L.

The Well's score is computed as follows:

Variable	Points
Clinical signs and symptoms of deep venous thrombosis	3.0
Alternative diagnosis less likely	3.0
Heart rate >100/min	1.5
Immobilisation	1.5
Previous pulmonary embolism or deep venous thrombosis	1.5
Haemoptysis	1.0
Malignancy (receiving treatment, treated within last 6 months or palliative)	1.0

Modified Wells score (mWS) of ≤ 4 = low risk patients, > 4 = high risk patients

Reference: Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost.* 2000;83 (3): 416–20.

Note: D-dimer is routinely elevated from the first trimester and gestational age normative D-dimer levels have not been sufficiently validated to allow their use as a risk stratification tool in pregnancy. Most pregnant women with no clinical evidence of DVT will have negative lower limb venous Doppler as pulmonary emboli originate in the pelvic veins, which are not accurately evaluated with duplex compression Doppler ultrasound. In such cases, ventilation perfusion lung scanning is the test of choice, due to lower breast dose than CTPA in pregnant women with suspected pulmonary embolism provided chest radiograph is normal and an alternative diagnosis such as neoplasia or aortic dissection, that are detectable with CT and not with VQ, is not suspected.

Supporting evidence

- Carrier M, Righini M, Wells P, et al. Subsegmental pulmonary embolism diagnosed by computed tomography: incidence and clinical implications. A systematic review and meta-analysis of the management outcome studies. *J Thromb Haemost* 2010;8(8):1716-2
- Ong CW, Malipatil V, Lavercombe M, et al. Implementation of a clinical prediction tool for pulmonary embolism diagnosis in a tertiary teaching hospital reduces the number of computed tomography pulmonary angiograms performed. *Intern Med J* 2013; 43(2):169-74
- Pasha SM, Klok FA, Snoep JD, et al. Safety of excluding acute pulmonary embolism based on an unlikely clinical probability by the Wells rule and normal D-dimer concentration: a meta-analysis. *Thromb Res* 2010; 125: e123-e127.
- van Es N, van der Hulle T, van Es J, et al. Wells rule and D-dimer testing to rule out pulmonary embolism. A systematic review and individual-patient data meta-analysis. *Ann Intern Med* 2016;165(4):253-6.
- Raja AS, Greenberg JO, Qaseem A, et al. Evaluation of patients with suspected acute pulmonary embolism: best practice advice from the clinical guidelines committee of the American College of Physicians. *Ann Intern Med* 2015;163:701–11.

How was this list created?

A panel of IMSANZ members produced an initial list of 32 low value tests, treatments and management decisions frequently encountered in general medicine services. This initial was distributed via e-mail to 350 members of a working group comprising approximately 50 general physicians as well as nurses and allied health professionals who ranked the items in terms of priority and were free to nominate additional items. Based on their responses, the list was condensed to 15 items including three which were not previously listed. These 15 items were the subject of a face-to-face forum of the working group which reached consensus on a final list of 10.

Recommendations on 'what not to do' were formulated around these 10 items and a summary of the evidence for each recommendation was prepared. An online survey based on this work was presented to and approved by IMSANZ Council. The survey was sent to all IMSANZ members asking respondents to assign a score from 1 to 5 for each recommendation on three criteria: 'The clinical practice being targeted by this recommendation is still being undertaken in significant numbers'; 'This recommendation is evidence-based'; and 'This recommendation is important in terms of reducing harm to patients and/or costs to the healthcare system'. The survey attracted 182 respondents from all across Australia and New Zealand, which was a response rate of 26%. The final top-five chosen were the recommendations with the five highest average total scores assigned to them.