

LETTERS

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PARACETAMOL, BACK PAIN, ARTHRITIS

Beware generalising results on paracetamol for low back pain

Machado and colleagues state that “paracetamol is ineffective in the treatment of low back pain” and base this conclusion on the analysis of three placebo controlled trials.¹ One of these trials has been retracted from the *European Journal of Anaesthesiology*.^{2,3}

The two remaining trials assess the efficacy of paracetamol in younger patients, mostly under 55 years of age, who have moderate to severe low back pain of less than six weeks’ duration.^{4,5} Care should be taken about generalising these findings to older patients and to those with chronic or persistent back pain, in whom satisfactory pain control can be particularly challenging to achieve.

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1 Machado GC, Maher CG, Ferreira PH, et al. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials. *BMJ* 2015;350:h1225. (31 March.)

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The reported modest improvement in pain scores among the study population suggests that some people would have had a good response to paracetamol. In addition, some study participants were taking low dose paracetamol, which could have reduced the effect size. This meta-analysis fails to consider the importance of paracetamol in a multimodal analgesic regimen and its potential to be opioid sparing.^{4,5}

Paracetamol may not benefit all patients, but it is useful for many. Given the lay media reporting of this study, patients may now be less willing to trial paracetamol and paradoxically be more likely to receive an NSAID or opioid. Is this the outcome we as healthcare professionals really want?

The management of persistent pain requires a pragmatic approach. Changing current guidelines on the basis of this meta-analysis without a more holistic consideration of the alternative options may be counterproductive. A trial of paracetamol remains an appropriate first line option for the management of persistent pain in most elderly patients.

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Paracetamol should remain first line option for persistent pain

Persistent pain in older people is a serious problem that is often undermanaged.¹ Osteoarthritis disproportionately affects older people, yet they are often under-represented in trials. Furthermore, their response to analgesics may differ from that of younger patients owing to altered pharmacokinetics and pharmacodynamics.²

The fundamental question raised by this meta-analysis is, if we dismiss paracetamol from our armamentarium, how do we manage persistent pain in elderly people?³

The alternatives are associated with serious problems. Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are associated with a large burden of adverse effects, particularly in elderly people. Paracetamol remains the safest option in this group. In addition, neither opioids nor NSAIDs have trial evidence supporting their long term use in persistent pain.

Authors’ reply

We understand Adam and Veal and Thompson’s desire to see a different result,¹⁻³ where the status of paracetamol as an effective pain relief could at least be preserved for elderly people or those with chronic conditions. Unfortunately their case is not consistent with the data.

Older people were not excluded from these studies and the lack of effect for osteoarthritis, a chronic condition, lends little hope to the belief that paracetamol would be effective for chronic back pain. We also disagree with the view that we should continue with paracetamol because it may work for some even if it does not work in general. The difficulty with this subgroup argument is that the effect of paracetamol was close to zero in the back pain trials. For there to be a subgroup in which paracetamol provides appreciable pain reduction, there needs to be a subgroup in which paracetamol appreciably increases pain. We think this is unlikely.

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SCREENING TESTS FOR TUBERCULOSIS

Limitations of TB screening tests in immunosuppression

We agree that a combination of an interferon γ release assay (IGRA; QuantiFERON-TB Gold in-Tube (QFT-IT) or TSPOT.TB) and a tuberculin skin test is the most sensitive approach to screening for latent tuberculosis infection in patients with rheumatological diseases before starting biological drugs.¹

The authors note that skin tests can be false-negative in patients receiving corticosteroids. However, IGRAs, which are designed primarily to achieve high specificity (versus high sensitivity), are also prone to false negative results in this setting.

A recent meta-analysis found no significant reduction in positive IGRA results in patients on corticosteroids, but the design and reported outcomes of included studies varied greatly.²

QFT-IT assays rely on detecting interferon γ induced by stimulation with tuberculosis specific antigens. QFT-IT produces “indeterminate” results if the interferon γ concentration in the negative control sample exceeds a predefined threshold or the interferon γ response in the positive control sample is insufficient.³ Our ex vivo study found that therapeutic levels of dexamethasone significantly reduce tuberculosis antigen induced interferon γ responses in the QFT-IT assay, without significantly reducing positive control responses (thereby not producing indeterminate results).⁴ Thus, patients receiving corticosteroids are at increased risk of false negative QFT-IT results.

Interestingly, we found that interferon γ inducible protein 10 was a more sensitive marker of latent tuberculosis in the presence of dexamethasone,⁴ which is consistent with a recent clinical study in immunosuppressed patients with rheumatoid arthritis.⁵

Until more robust and more accurate immune based tuberculosis tests become available, we strongly endorse the recommendation that a combination of tuberculin skin test and IGRA

should be used to determine the tuberculosis infection status of immunosuppressed patients.¹ Even this cautious approach cannot definitively exclude the presence of latent tuberculosis in this setting.

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1 Hewitt RJ, Francis M, Singanayagam A, et al. Screening tests for tuberculosis before starting biological therapy. *BMJ* 2015;350:h1060. (5 March.)

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Author's reply

Clifford and colleagues' data from an ex vivo model indicating that dexamethasone suppresses the interferon γ response to tuberculosis antigen but not the mitogen control response adds further strength to the clinical merits of using a "dual testing" approach.^{1,2}

Interest has been shown in the use of interferon γ inducible protein 10, rather than interferon γ , as a potential marker,³ and clinical studies are needed to validate its clinical utility.

We agree that continued vigilance is needed even when IGRA and the tuberculin skin test are both negative given each test's limitations in inflammatory disease and immunomodulation.

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HIV HEALTH TOURISM

Time to end the political rhetoric on health tourism

The recent news article that systematically refuted Nigel Farage's allegations of so called HIV health tourism is commendable.¹

Farage's comments undermine public health efforts to tackle the rising incidence of HIV infections in the UK. Most migrants seek HIV testing only after symptom onset.² UKIP's anti-immigrant rhetoric will further stigmatise migrants when we need to increase rates of diagnosis.

The article correctly questions the evidence for HIV health tourism. We would argue that the entire premise of health tourism is unfounded. The current government has been "unable to estimate" the number of health tourists

entering the UK, instead basing its figures on an absurd theoretical calculation.³ Evidence of health tourism from the front line is equally lacking: Doctors of the World reported that only 1.6% of migrants at its London clinic left their country for health reasons; most are here to work, study, or escape persecution.⁴

Migrants remain indispensable to society, with a net contribution to the UK economy through skilled employment and tax contributions. The NHS faces far bigger problems than that of health tourism: it is time to end the political rhetoric.

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1 Kmietowicz Z. UKIP wrong about HIV data and health tourism, say campaigners. *BMJ* 2015;350:h1943. (13 April.)

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NEW UK LAW ON CONSENT

Clarifying Montgomery judgment

Many doctors have questioned the implications of the recent Supreme Court judgment of *Montgomery v Lanarkshire Health Board* on the way they obtain a patient's consent.^{1,2}

When discussing benefits and risks of treatment, the new ruling requires doctors to consider whether "a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it."

Undoubtedly doctors will want to reflect on the information given to patients about treatment risks. However, rather than leading to a radical change in practice, as some have suggested, the judgment brings the law in line with current ethical guidance for UK doctors.

Since 2008, General Medical Council guidance on consent has underlined the need to obtain patients' informed consent.³ Doctors should focus their discussions on the individual situation and risk to the patient. Doctors are required to tell patients if an investigation or treatment might result in a serious adverse outcome, even if the likelihood is very small.

The judgment recognises this individual approach to warning patients about risk. Rather than just taking into account the percentage possibility of a risk arising, doctors need to consider the nature of the risk and the effect it would have on that particular patient's life if it occurred. The assessment should be both fact sensitive and sensitive to the characteristics of the particular patient.

For patients to be best able to retain and comprehend the information, doctors should

explain risks and side effects in non-technical language, and whenever possible discussions should occur in a place and at a time that helps this process.

The Medical Defence Union has published further information in a blog.⁴

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1 Uzoigwe OF. Consent forms for "no surgery" as ramification of landmark ruling. *BMJ* 2015;350:h1796. (7 April.)

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URGENT CARE AND PRIMARY CARE

Primary care is not urgent care, and we need more urgent care

Loxterkamp argues that general practices are better than urgent care centres for treating urgent problems.¹ This has relevance in the UK. The current government was advised by GPs who shared Loxterkamp's view and closed down many GP led (Darzi) health centres. This made neither economic nor ethical sense.

A recent survey showed that the Sheffield Darzi centre was responsible for a significant reduction in emergency department attendances in 2010.² I was its clinical director at the time and campaigned to incorporate new skills and technology as a means to increase this impact. Unfortunately the owners were not prepared to take this next step.

My belief that most people can get a GP appointment quickly if needed was shattered in Sheffield. Even with the best appointment systems, many patients lacked the skill to negotiate an appointment. The homeless, those with English as a second language, and sick patients without energy fared badly.

Urgent care centres satisfy ethical principles well. Timely assessment reduces clinical risk. Comprehensive treatments that complete care at the first attendance provide direct benefit. Popular care options respect patients' autonomy rather than doctors' prejudices. And making care available to people when they walk in distributes resources more justly than putting up barriers that favour the better educated and more pushy.

The UK has an emergency medicine crisis, with increasingly more patients needing treatment beyond the scope of general practice. Much of this is within the scope of urgent care centres, which could do the work more cheaply, without denuding our stretched emergency care service. The convenient truth is that primary care is not good urgent care, and we need more of the latter.

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1 Loxterkamp D. An inconvenient truth: urgent care is not primary care. *BMJ* 2015;350:h1657. (26 March.)

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