Electronic health record alerts for acute kidney injury

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Study question Does an automated, electronic alert for acute kidney injury for patients in hospital reduce the rate of progression of acute kidney injury, dialysis, or death?

Methods 6030 adult inpatients with acute kidney injury across six medical centres in the Yale New Haven Health System in Connecticut and Rhode Island, US, were enrolled in this double blinded, multicentre, parallel, randomised controlled trial of an electronic alert versus usual care (no alert). The primary outcome was a composite of progression of acute kidney injury, receipt of dialysis, and death.

Study answer and limitations The primary outcome occurred in 653 (21.4%) of 3059 patients with an alert and 622 (20.9%) of 2971 patients receiving usual care (relative risk 1.02, 95% confidence interval 0.93 to 1.13, P=0.67). Analysis by each hospital showed worse outcomes in the two non-teaching hospitals (n=765, 12.7%), where alerts were associated with a higher risk of the primary outcome (relative risk 1.49, 95% confidence interval 1.12 to 1.98, P=0.006). More deaths occurred at these centres (15.6% in the alert group v 8.6% in the usual care group, P=0.003). The study was limited in that the alert did not provide patient specific recommendations.

What this study adds This randomised controlled trial found no overall effect on the risks of death, dialysis, or disease progression in patients in hospital with acute kidney injury, but did detect significant heterogeneity of the effect of the alert across hospitals.

Funding, competing interests, and data sharing Funded by a grant from the National Institute of Diabetes, Digestive, and Kidney Diseases. Full details of competing interests are on bmj.com. A deidentified participant dataset with an associated data dictionary can be found at https://doi.org/10.5061/dryad.4f4qrfj95.

Study registration ClinicalTrials.gov NCT02753751.
Antidepressants for musculoskeletal pain

ORIGINAL RESEARCH Systematic review and meta-analysis

Efficacy and safety of antidepressants for the treatment of back pain and osteoarthritis

Ferreira GE, McLachlan AJ, Lin C-WC, et al
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Study question How efficacious and safe are antidepressants for back pain, sciatica, and osteoarthritis?

Methods This systematic review identified randomised trials that tested the efficacy of antidepressants compared with placebo in people with back pain (low back and neck pain with or without radicular symptoms) and osteoarthritis (hip or knee). Primary outcomes were pain and disability (0–100 scale, with 0 representing no pain or disability). Safety was the secondary outcome (any adverse event, serious adverse events, proportion of participants who withdrew from trials because of adverse events).

Study answer and limitations Serotonin-noradrenaline reuptake inhibitors (SNRIs) significantly reduced back pain (mean difference −5.30, 95% confidence interval −7.31 to −3.30), disability due to back pain at 3–13 weeks (−3.55, −5.22 to −1.88), as well as osteoarthritis pain (−9.72, −12.75 to −6.69) and disability (6.07, −8.13 to −4.02) compared with placebo in people with back pain and osteoarthritis. Effects were, however, small and unlikely to be clinically important. SNRIs and tricyclic antidepressants might be effective for sciatica, but the certainty of evidence ranged from low to very low. Limitations include uncertainty in the effects for sciatica and safety outcomes and lack of efficacy and safety data beyond six months.

What this study adds Findings suggest that the effects of SNRIs are too small to be clinically important for back pain and osteoarthritis. SNRIs and tricyclic antidepressants might offer clinically important benefits for sciatica, but these findings are much less certain.

Funding, competing interests, and data sharing This research received no specific grant from any funding agency. Competing interests include support from the following organisations that might have an interest in the submitted work in the previous three years: GlaxoSmithKline (postgraduate scholarship), Pfizer (investigational products for two investigator initiated National Health and Medical Research Council funded trials), and Flexeze (provision of heat packs at no cost for a trial). No additional data available.

Systematic review registration PROSPERO CRD42020158521.

COMMENTARY People need help to live better with their pain, without prescription drugs

Back pain, neck pain, and osteoarthritis are leading causes of disability globally.1 Although non-drug treatments are the preferred first option for such pain and disability, a role remains for drug treatments.2,3 The impact of the opioid prescribing epidemic and the challenges of helping those affected are well known.4 Opioid prescribing is decreasing while gabapentinoid use is increasing, despite a weak evidence base and known harms.5 In this issue the paper by Ferreira and colleagues reporting a well conducted systematic review of trials of antidepressants for these musculoskeletal disorders is timely.6

The authors set a difference of 10 points on a 100 point scale for pain or disability as the smallest worthwhile difference between groups—a threshold commonly used in studies of chronic pain.7 It is also the smallest worthwhile individual treatment benefit from non-steroidal anti-inflammatory drugs or physiotherapy for chronic low back pain.8 This distinction is important since a modest overall benefit at group level could still mean that a some treated individuals gain a worthwhile benefit.9

For back pain, pooled data from four industry sponsored trials of duloxetine showed effect sizes substantially smaller than the authors’ prespecified worthwhile between group difference. The 95% confidence intervals effectively excluded any possibility that such an effect size was achieved. For tricyclic antidepressants, the mean difference for pain at 3–13 weeks was −9.9 (95% confidence interval −21.50 to 1.58); although this might not be enough to support the use of these drugs, a worthwhile effect from tricyclic antidepressants has not been excluded. Both findings are consistent with UK National Institute for Health and Care Excellence guidance against the use of antidepressants for low back pain.10 The American College of Physicians’ guidance, however, suggests considering duloxetine as second line drug treatment for chronic low back pain.11

Antidepressants for sciatica

It is not possible to draw any conclusions from the limited data on the use of antidepressants for radicular pain (sciatica). This is of concern when antidepressants might be expected to improve neuropathic pain such as sciatica through central modulation of pain, and when both amitriptyline and duloxetine are recommended by the relevant NICE guidance.12 The lack of evidence supporting drugs already widely prescribed for sciatica is perhaps surprising, and more work is needed to confirm or refute the place of these drugs in our armamentarium.

All the osteoarthritis trials included by Ferreira and colleagues tested treatments for knee osteoarthritis; largely industry

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1. Institute for UK National

2. Ferreira and colleagues tested trials of antidepressants for back pain and osteoarthritis; SNRIs and tricyclic antidepressants might offer clinically important benefits for sciatica, but these findings are much less certain.

3. Funding, competing interests, and data sharing This research received no specific grant from any funding agency. Competing interests include support from the following organisations that might have an interest in the submitted work in the previous three years: GlaxoSmithKline (postgraduate scholarship), Pfizer (investigational products for two investigator initiated National Health and Medical Research Council funded trials), and Flexeze (provision of heat packs at no cost for a trial). No additional data available.

4. Systematic review registration PROSPERO CRD42020158521.
sponsored studies of duloxetine. Pooled data from eight studies found an effect on pain at 3-13 weeks of −9.72 (−12.57 to −6.69) meaning that a worthwhile effect has not been excluded. NICE does not make a specific recommendation on antidepressants for osteoarthritis. Osteoarthritis Research Society International (OARSI) guidance does, however, make a conditional recommendation for the use of duloxetine by people with osteoarthritis and widespread pain or depression.

Making sense of the evidence and inconsistent recommendations in this area is challenging. For example, draft NICE guidance is to consider antidepressants for chronic pain but not for chronic sciatica. A robust overview is needed to clarify guidance and to inform a consistent approach to use of antidepressants for people with painful disorders. Many people with chronic pain also have symptoms of depression. Any such overview should consider the potential for reducing depressive symptoms. We cannot tell from Ferreira and colleagues’ review how many individuals gained a worthwhile benefit from their drug treatment. Despite the reported small effects at group level, some individuals with back pain or osteoarthritis may gain a personal benefit from serotonin-noradrenaline reuptake inhibitors (SNRIs). Absolute effect sizes for physical treatments for low back pain are of similar magnitudes to those reported here and translate into numbers needed to treat of between 5 and 9. If the same were true for SNRIs, some people might choose to a try that option for a chance of a worthwhile reduction in pain after three months. They can easily stop if treatment is ineffective or does not suit them. As others put it: “Expect analgesic failure; pursue analgesic success.”

Overall, however, drug treatments are largely ineffective for back pain and osteoarthritis and have the potential for serious harm. We need to work harder to help people with these disorders to live better with their pain without recourse to the prescription pad.

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**Home and Online Management and Evaluation of Blood Pressure (HOME BP) using a digital intervention in poorly controlled hypertension**

McManus RJ, Little P, Stuart B, et al

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**Study question** Can a digital intervention for hypertension management in primary care that combines self-monitoring of blood pressure with guided self-management lead to lower systolic blood pressure after one year?

**Methods** 622 people with treated but poorly controlled hypertension (>140/90 mm Hg) and access to the internet were randomised to the HOME BP (Home and Online Management and Evaluation of Blood Pressure) intervention or usual care. The HOME BP intervention was an integrated patient and healthcare practitioner online digital intervention, including training, blood pressure self-monitoring with monitors provided by the study, healthcare practitioner directed titration of antihypertensive drugs, and lifestyle modifications selected by the patient. Usual care was routine hypertension care, with appointments and drug changes made at the discretion of the patient’s general practitioner. The primary outcome was the difference in systolic blood pressure (mean of second and third readings) after one year, adjusted for baseline blood pressure, blood pressure target, age, and practice (as a random effect to take into account clustering), with multiple imputation for missing values.

**Study answer and limitations** After one year, data were available from 552 participants (88.6%) with imputation for the remaining 70 participants (11.4%). Mean blood pressure decreased from 151.7/86.4 to 138.4/80.2 mm Hg in the intervention group and from 151.6/85.3 to 141.8/79.8 mm Hg in the usual care group, giving a mean difference in systolic blood pressure of −3.4 mm Hg (95% confidence interval −6.1 to −0.8 mm Hg) and a mean difference in diastolic blood pressure of −0.5 mm Hg (−1.9 to 0.9 mm Hg). Results were comparable in the complete case analysis, and adverse effects were similar between groups. Within trial costs showed an incremental cost effectiveness ratio of £11 (€12, $15; 95% confidence interval £6 to £29) per mm Hg reduction. The major limitations were that the intervention required online access and self-monitoring equipment, which might not be available to the whole population, and that subgroup analysis suggested a reduction in effect in older people (≥67 years).

**What this study adds** The HOME BP digital intervention for the management of hypertension by using self-monitored blood pressure led to better control of systolic blood pressure after one year than usual care.

**Funding, competing interests, and data sharing** Funded by the National Institute for Health Research. Omron provided the monitors used in the HOME BP trial at reduced cost. Full details on funding and competing interests are on bmj.com. Anonymised trial data are available on reasonable request.

**Trial registration** ISRCTN13790648.