Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors; a review of the evidence for an American pain society and American academy of pain medicine clinical practice guideline

Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK

CRD summary
Evidence on instruments to predict or identify aberrant drug-related behaviours in patients who used opioids for chronic non-cancer pain was sparse and of relatively poor quality. There was a need for further research to identify useful screening tools. There were methodological weaknesses in this review but the authors' cautious conclusions and the recommendations for further research seem appropriate.

Authors' objectives
To review methods to predict and identify aberrant drug-related behaviours when opioids are used for chronic non-cancer pain.

Searching
MEDLINE, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception through July 2008 (search terms reported). Reference lists and citations suggested by experts were checked. Only full papers published in English were considered for inclusion.

Study selection
Studies were included where the population was adults (over 18 years) with chronic non-cancer pain and fulfilled one of three sets of criteria: prospective studies that reported on the ability of risk stratification instruments to predict aberrant drug-related behaviours; studies that evaluated the accuracy of monitoring instruments, urine drug screens, prescription drug monitoring, blood level monitoring and pill counts to identify current aberrant drug-related behaviours; and randomised controlled trials (RCTs) or controlled observational trials that evaluated the effects of risk stratification or monitoring strategies on specified patient outcomes.

Studies that evaluated the accuracy of screening instruments to predict aberrant drug-related behaviour used three self-administered instruments that were variations of Screener and Opioid Assessment for Patients with Pain (SOAPP). The total number of risk assessment items ranged from 10 to 24. Loss to follow-up ranged from 20% to more than 40% or was unclear. Baseline severity of pain was poorly reported and the populations included patients only on chronic opioids, starting on opioids or a mixture of both.

Studies that evaluated the accuracy of screening instruments to identify current aberrant drug-related behaviour used different instruments; only the Pain Medication Questionnaire was used more than once. Of the eight instruments evaluated, two were self-administered, four were interviewer-administered and two were not reported clearly. The number of items per instrument varied from three to 42. Only one study reported pain scale scores. No studies reported opioid doses prescribed.

A few studies reported on the accuracy of urine drug screening to detect drug use or reduce aberrant drug-related behaviours. These used historical controls and little data was presented on patient characteristics.

No studies were found for: effectiveness of risk assessment and monitoring for reducing risk or improving outcomes; effectiveness of pill counts, limited prescriptions, blood levels, prescription drug monitoring; and effectiveness of monitoring at different intervals.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
Two reviewers independently rated the quality of each study. Discrepancies were resolved by discussion and consensus. Risk prediction and diagnostic test accuracy studies were assessed according to nine criteria adapted from published...
studies and checklists. Studies that met at least five of the nine criteria were considered to be of higher quality.

**Data extraction**
Sensitivity and specificity values were calculated for each study with available data. Positive and negative likelihood ratios and diagnostic odds ratios (DOR) were derived. Where the cell of a 2x2 table had zero events, 0.5 was added to all cells to enable the calculations.

The authors did not report how many reviewers performed the data extraction.

**Methods of synthesis**
A narrative synthesis was based on methods from the US Preventative Services Task Force. The overall strength of the evidence was rated as good, fair or poor based on the number, quality and size of the studies, consistency of results and directness of the evidence. Positive likelihood ratios of more than 10 and negative likelihood ratios of 0.1 or less were classed as large/strong. Positive likelihood ratios from more than 5 to 10 and negative likelihood ratios from more than 0.1 to 0.2 were classed as moderate. Positive likelihood ratios from more than 2 to 5 and negative likelihood ratios from more than 0.2 to 0.5 were classed as small/weak.

**Results of the review**
Sixteen studies were included in the review: four evaluated risk prediction instruments; nine reported on monitoring instruments; one focused on the accuracy of urine drug screening; and two looked at the effect of urine drug screening or adherence monitoring on clinical outcomes.

Four prospective studies (658 participants at follow-up) evaluated the three different self-administered screening instruments to predict aberrant drug-related behaviours. Reported follow-up ranged from five to 12 months. Quality ranged from 4 to 6 out of 9. Three of the four studies were considered as higher quality but none met all of the quality criteria and important methodological shortcomings were identified. Overall there was fair to poor evidence that high scores on the SOAPP version 1 (negative likelihood ratio 0.13, 95% CI 0.05 to 0.34) and SOAPP-R (negative likelihood ratio 0.29, 95% CI 0.18 to 0.46) increased the likelihood of future aberrant drug-related behaviour and low scores tended to decrease such future behaviours.

Nine studies (1,530 participants) evaluated the accuracy of screening instruments in identifying aberrant drug-related behaviours. Five studies met the higher quality threshold. All studies had methodological shortcomings. There was fair to poor evidence from one study that scores on Current Opioid Misuse Measure scale weakly predicted the absence or presence of drug-related aberrant behaviours (positive likelihood ratio 2.77, 95% CI 2.06 to 3.72 and negative likelihood ratio 0.35, 95% CI 0.24 to 0.52). Studies of other monitoring instruments did not report diagnostic accuracy, found poor diagnostic accuracy or were difficult to interpret due to methodological problems.

One retrospective study (226 participants) analysed the accuracy of drug urine screening carried out with gas chromatography-mass spectrometry compared to self-report. Although sensitivities were reported the results were unclear as it was uncertain who was blinded in the study and when drug use last occurred relative to the timing of urine sampling.

Two observational studies reported on prevalence of drug use in settings where random drug urine screening or agreed adherence monitoring was implemented. Although both studies appeared to suggest these measures reduced aberrant behaviours, the results were difficult to interpret due to poor reporting of statistical differences, use of historical controls and inadequate description of the monitoring protocols.

**Authors’ conclusions**
Evidence on instruments to predict or identify aberrant drug-related behaviours in patients who used opioids for chronic non-cancer pain was limited. Several screening tools may be useful but further high quality research was required to overcome methodological limitations.

**CRD commentary**
This review addressed a broad but clear question with defined inclusion criteria. The search covered relevant databases. Exclusion of papers that were unpublished or in languages other than English was likely to have introduced publication bias.
and language biases, but the authors felt this was unlikely to have influenced their results. Methodological processes were poorly reported so it was unclear how many reviewers performed study selection and data extraction. Two reviewers independently assessed study quality. Use of a narrative synthesis appeared appropriate and this was carried out taking into account study validity, setting and generalisability.

There were methodological weaknesses in this review but the authors’ cautious conclusions and recommendations for further research seem appropriate.

**Implications of the review for practice and research**

*Practice:* The authors did not state any implications for practice in this paper (see Other Publications of Related Interest).

*Research:* The authors recommended that future research should be methodologically rigorous, use standardised definitions for relevant behaviours, externally validate previously derived instruments and evaluate the impact of monitoring characteristics on patient outcomes. Research of the accuracy and effectiveness of using urine drug screens, pill counts and prescription monitoring programmes was scarce.

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