2015

The use of paracetamol (acetaminophen) among a community sample of people with chronic non-cancer pain prescribed opioids

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**Publication Details**


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Abstract

Background
The regular use of simple analgesics in addition to opioids such as paracetamol (or acetaminophen) is recommended for persistent pain to enhance analgesia. Few studies have examined the frequency and doses of paracetamol among people with chronic non-cancer pain including use above the recommended maximum daily dose.

Aims
To assess (i) the prevalence of paracetamol use among people with chronic non-cancer pain prescribed opioids, (ii) assess the prevalence of paracetamol use above the recommended maximum daily dose and (iii) assess correlates of people who used paracetamol above the recommended maximum daily dose including: age, gender, income, education, pain severity and interference, use of paracetamol/opioid combination analgesics, total opioid dose, depression, anxiety, pain self-efficacy or comorbid substance use, among people prescribed opioids for chronic non-cancer pain.

Methods
This study draws on baseline data collected for the Pain and Opioids IN Treatment (POINT) study and utilises data from 962 interviews and medication diaries. The POINT study is national prospective cohort of people with chronic non-cancer pain prescribed opioids. Participants were recruited from randomly selected pharmacies across Australia.

Results
Sixty-three per cent of the participants had used paracetamol in the past week (95% CI = 59.7–65.8). Among the paracetamol users 22% (95% CI = 19.3–24.6) had used paracetamol/opioid combination analgesics and 4.8% (95% CI = 3.6–6.3) had used paracetamol above the recommended maximum daily dose (i.e. > 4000 mg/day). Following binomial logistic regression ($\chi^2 = 25.98$, df = 10, p = 0.004), people who had taken above the recommended maximum daily dose were less likely to have low income (AOR = 0.52, 95% CI = 0.27–0.99), more likely to use paracetamol/opioid combination analgesics (AOR = 2.01, 95% CI = 1.02–3.98) and more likely to take a higher opioid dose (AOR = 1.00, 95% CI = 1.00–1.01).

Conclusion
The majority of people with chronic non-cancer pain prescribed opioids report using paracetamol appropriately. High income, use of paracetamol/opioid combination analgesics and higher opioid dose were independently associated with paracetamol use above the recommended maximum daily dose.

Keywords
sample, prescribed, pain, community, non-cancer, chronic, people, among, (acetaminophen), opioids, paracetamol

This journal article is available at Research Online: https://ro.uow.edu.au/sspapers/4180
The use of paracetamol (acetaminophen) among a community sample of people with chronic non-cancer pain prescribed opioids

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SUMMARY

Background: The regular use of simple analgesics in addition to opioids such as paracetamol (or acetaminophen) is recommended for persistent pain to enhance analgesia. Few studies have examined the frequency and doses of paracetamol among people with chronic non-cancer pain including use above the recommended maximum daily dose. Aims: To assess (i) the prevalence of paracetamol use among people with chronic non-cancer pain prescribed opioids, (ii) assess the prevalence of paracetamol use above the recommended maximum daily dose and (iii) assess correlates of people who used paracetamol above the recommended maximum daily dose including: age, gender, income, education, pain severity and interference, use of paracetamol/opioid combination analgesics, total opioid dose, depression, anxiety, pain self-efficacy or comorbid substance use, among people prescribed opioids for chronic non-cancer pain. Methods: This study draws on baseline data collected for the Pain and Opioids IN Treatment (POINT) study and utilises data from 962 interviews and medication diaries. The POINT study is national prospective cohort of people with chronic non-cancer pain prescribed opioids. Participants were recruited from randomly selected pharmacies across Australia. Results: Sixty-three per cent of the participants had used paracetamol in the past week (95% CI = 59.7–65.8). Among the paracetamol users 22% (95% CI = 19.3–24.6) had used paracetamol/opioid combination analgesics and 4.8% (95% CI = 3.6–6.3) had used paracetamol above the recommended maximum daily dose (i.e. > 4000 mg/day). Following binomial logistic regression (χ² = 25.98, df = 10, p = 0.004), people who had taken above the recommended maximum daily dose were less likely to have low income (AOR = 0.52, 95% CI = 0.27–0.99), more likely to use paracetamol/opioid combination analgesics (AOR = 2.01, 95% CI = 1.02–3.98) and more likely to take a higher opioid dose (AOR = 1.00, 95% CI = 1.00–1.01). Conclusion: The majority of people with chronic non-cancer pain prescribed opioids report using paracetamol appropriately. High income, use of paracetamol/opioid combination analgesics and higher opioid dose were independently associated with paracetamol use above the recommended maximum daily dose.

Introduction

Chronic pain is a highly prevalent condition that imposes a considerable burden on individuals and the wider community. In Europe and the USA, the prevalence of chronic pain is approximately 19% (1) and 31% (2) respectively. In Australia, chronic pain affects approximately 17% of women and 20% of men (3). There have been dramatic increases in the use of prescription opioids, for example from...
1992 to 2007, opioid prescriptions in Australia increased by 300% (4). Despite the common use of opioids for chronic non-cancer pain (CNCP), qualitative and quantitative reviews of opioid use in chronic pain report that opioids may reduce pain by 30%, or 2–3 points on a 10 point analogue visual scale (5–7), suggesting that opioid medications alone may not provide adequate pain relief.

Paracetamol is relatively inexpensive, readily available and has minimal risk of adverse events when used at recommended doses (8,9). Use of paracetamol in conjunction with opioids can enhance analgesia (9,10) and the World Health Organization’s (WHO) three-step pain ladder (though originally developed for cancer pain, the recommendations are considered appropriate for other types of pain) (11) recommends that at Step 2 and 3, round-the-clock dosing of both opioid medication and adjuvant medications that enhance analgesia (including paracetamol) be used (12). However, use of paracetamol above the recommended maximum daily dose (greater than 4000 mg/day) can cause adverse effects (13–15). Although paracetamol is commonly used in practice, to date, there is a lack of literature describing the frequency of use, the range of dosages and frequency of inappropriate use in people with CNCP.

Recently, the United States Food and Drug Administration (FDA) have limited the amount of paracetamol per tablet in paracetamol/opioid combination analgesics to 325 mg instead of 500 mg. This change has been made because studies on paracetamol overdoses in the USA have reported that almost half of paracetamol overdoses are unintentional and a large proportion of overdoses occur from combination products (16, 17). Studies have also reported that 19% of people in the USA prescribed paracetamol/opioid combination analgesics were at risk of liver toxicity because of prescriptions exceeding the maximum recommended daily dose of paracetamol (13) and that prescriptions exceeding 4000 mg/day accounted for 6–8% of all paracetamol/opioid combination prescriptions (13,18). Literature on the associations of paracetamol and other over the counter medication use, report that those who exceed the maximum daily dose are more likely to have current pain, to be taking opioids or be prescribed more types of analgesics, to have depression and anxiety and to currently smoke cigarettes (19–21).

To date, there has been minimal literature on paracetamol use and the subset of inappropriate paracetamol use in people with CNCP prescribed opioids. Specifically, this study aims to examine: (i) the prevalence of paracetamol use in people with CNCP prescribed opioids, as well as the range of dosages and the types of combination products used (ii) the prevalence of paracetamol use above the recommended maximum daily dose and (iii) whether demographic characteristics, pain severity and interference with daily activities, use of paracetamol/opioid combination analgesics, total opioid dose, mental health and comorbid substance use, are associated with paracetamol use above the recommended maximum daily dose.

Methods

Study Design

This paper uses data from the Pain and Opioids IN Treatment (POINT) study. The POINT study is a national prospective cohort that aims to follow 1500 people with CNCP prescribed opioids over a 24-month period. For a detailed description of the POINT study protocol, see Campbell et al. (22). In brief, participants were recruited from randomly selected Australian pharmacies. Eligible
participants had chronic pain (defined as persistent pain for 3 months or more), were currently prescribed opioids for at least 6 weeks, were not currently suffering from cancer, and were not currently undergoing opioid substitution treatment for the management of opioid dependence developed through heroin use.

The major aims of the POINT study are to examine the natural history of prescribed opioid use; examine the predictors of adverse events; and identify factors that predict poor self-reported pain relief and other outcomes. The study was approved by the Human Research Ethics Committee of the University of New South Wales (HREC reference: # HC12149).

Recruitment

Research staff randomly contacted 5532 pharmacies (93% of pharmacies across Australia) for expressions of interest to recruit for the study, 1868 (34%) agreed to help with recruitment and of those pharmacies that agreed to recruit, 480 (26%) actively recruited. Pharmacists were asked to hand out flyers to customers who came into the pharmacy to fill a Schedule 8 opioid prescription and interested customers then left their details for contact by the research team to be made. Schedule 8 opioids are opioids subject to strict regulatory controls regarding their manufacture, supply, distribution, possession and use (23). These opioids included: buprenorphine, codeine (30 mg codeine tablets or codeine linctus), fentanyl, hydromorphone, morphine and oxycodone.

From this referral method, 2318 people expressed an interest, 1262 (54%) participated in the study, 310 (13%) were ineligible, 343 (15%) refused to participate and 403 (17%) could not be contacted. Of those who were ineligible, 132 (43%) felt they were too unwell to participate, 9 (3%) did not speak English, 105 (34%) had not been prescribed opioids for 6 weeks, 40 (13%) were suffering from cancer, six (2%) were receiving opioid substitution treatment for heroin dependence and 18 (6%) did not meet study criteria for suffering from chronic pain (defined as pain lasting 3 months or longer). Of the participants who completed the baseline interview and had adequate time to complete and return the study pack, 962 (74%) returned the medication diary.

Medication use

Daily dose and days of use in the past week for all prescribed and non-prescribed medications were collected via a 1 week self-complete medication diary, which participants were asked to complete in the same week that they completed the phone and baseline self-report survey. A total daily paracetamol dose was calculated from the medication diary for each person by adding the dose of paracetamol present in all paracetamol-containing medications (including combination products) for each day in the last week. Use above 4000 mg on any day was considered use above the recommended maximum daily dose (24).

A protocol for converting the mean daily opioid doses to oral morphine equivalent dose was constructed for the POINT study (see Appendix 1) (25). A mean daily dose was calculated for each opioid medication by dividing the total weekly dose by the number of days of use. The mean daily doses for each of the opioids were converted to oral morphine equivalent doses (in milligram

The oral morphine equivalent doses were then added together to create a total daily opioid dose. Dose conversion ratios were cross-checked from the Therapeutic Guidelines (26), Australian Medicines Handbook (27) and a consensus document developed by the faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists (FPMANZCA). Where there was non-concordance between the three references, precedence was given to recommendations by the Therapeutic Guidelines and in the case of methadone, Walker et al. (28) was used for calculating oral morphine equivalent doses.

**Covariates**

Participant demographics were self-report variables obtained from the baseline phone interview and included age, gender, education, chronic pain condition and current income. Income was reported as greater than or less than/equal to $399/week, which is approximately equivalent to the weekly allowance of government pensions. Also used in the analysis were baseline interview variables from the: Brief Pain Inventory (BPI) for pain severity and interference (29); Patient Health Questionnaire 9 item (PHQ9) scale for Depression (30,31); Generalized Anxiety Disorder 7 item (GAD-7) scale (32); the Pain Self-Efficacy Questionnaire (PSEQ) (33) and the Opioid-Related Behaviours in Treatment (ORBIT) scale (34).

**Pain severity and interference**

The BPI measures pain severity using an 11 point scale and participants rate the worst, least and average pain experienced in the last week as well as current pain level. These measures are presented individually and as a total mean pain severity score. The BPI also measures the degree of relief provided by all medications and treatments provided in the last week as a percentage. Participants also rate the level of interference pain causes to activities on an 11 point scale; including general activity, mood, walking ability, work, relationships, sleep and enjoyment of life. A mean interference score was then calculated for participants who answered 50% or more of the questions (29,35,36).

**Symptoms of anxiety and depression**

PHQ-9 and GAD-7 measure the severity of the 9 DSM-V depressive symptoms and 7 symptoms of anxiety over the last 2 weeks. The severity of depression or anxiety was calculated by the sum of scores for each response to a symptom of depression or anxiety. PHQ-9 and GAD-7 scores greater than 10 meet criteria for moderate to severe depression or anxiety symptoms (30,31).

**Pain self-efficacy questionnaire**

All participants were asked 10 questions regarding their confidence to do a variety of activities ‘despite their pain’. The activities included physical activities (completing chores, working, becoming more active and socialising) as well as emotional experiences (accomplishing goals, coping with pain
Aberrant opioid-related behaviours

All participants were asked 10 questions regarding aberrant opioid-related behaviours over the preceding 3 months. These were scored dichotomously and added to give a total score using the Opioid-Related Behaviours in Treatment (ORBIT) scale (e.g. ‘Over the past 3 months, I have asked my doctor for an increase in my prescribed dose’). The ORBIT scale was developed for use among Australian people receiving opioids for pain or opioid dependence in both clinical and research settings. The scale has demonstrated strong internal consistency (Cronbach’s alpha = 0.85) (34).

Statistical analysis

Analyses were conducted using IBM SPSS statistics version 22 (SPSS, Inc., Chicago, IL, USA). At bivariate level, continuous variables were compared with paracetamol use below and above the recommended maximum daily dose using the independent samples t-test and Mann–Whitney U for all non-normally distributed variables. Categorical variables were compared using odds ratios (ORs). All significance tests were two-sided and conducted at a 0.05 significance level. A logistic regression analysis was used to examine predictors of paracetamol use in excess of maximum recommended daily doses. Variables that were included in the model were demographic variables (sex and age) and all variables in the bivariate analysis that had a p-value less than 0.25. Linearity assumption tests (37) were also conducted for all continuous variables in the model using the BoxTidwell (1962) procedure (38).

Results

Demographics and health characteristics

The mean age of the participants was 59 years (SD 13.3) and ranged from 21 to 94 years. Over half were female (57%, 95% CI = 53.4–59.7), about one-third (34%, 95% CI = 31.4–37.4) were retired, 47% (95% CI = 43.6–50.2) were unemployed and 60% (95% CI = 57.3–63.4) had a weekly income of $399 or less. Almost two-thirds (61%, 95% CI = 58.2–63.4) reported changing their employment in some way because of their pain condition. Participants had been living with chronic pain for a median of 10 years (ranging between 0 and 72 years) and 73% (95% CI = 70.6–76.2) have had two or more problematic chronic pain conditions in the last 12 months. In addition to experiencing chronic pain, 51% (95% CI = 48.1–54.4) of participants reported having an additional problematic physical condition in the last 12 months, for example, problems relating to stroke, heart attack, sleep apnoea, heart disease, hypertension, chronic respiratory diseases, diabetes, HIV, epilepsy, seizures and cancer. Furthermore, 44% (95% CI = 41.1–47.3) met criteria for current moderate to severe
depression and 22% (95% CI = 18.8–24.0) met criteria for current moderate to severe generalised anxiety disorder (Table 1).

Medication use

The most commonly used opioids were oxycodone (56%, 95% CI = 52.7–58.9) and buprenorphine (21%, 95% CI = 18.8–24.0; Table 2). In addition, 25% (95% CI = 22.5–28.0) were taking another opioid, with codeine combinations (17%, 95% CI = 14.9–19.7) the most common. The median total daily opioid dose was 68 mg (IQR = 106 mg) and ranged from 0 mg to 800 mg. In addition to the opioids, over half of all participants (56%, 95% CI = 52.3–58.6) had taken antidepressants and a quarter had taken antiepileptic (27%, 95% CI = 24.0–29.6) or benzodiazepine medications (26%, 95% CI = 23.6–29.2) in the last week.

In addition to prescribed medications, 64% (95% CI = 60.5–66.7) of participants also reported using over the counter strength analgesic medications in the last week, with the most prevalent being medications containing paracetamol (50%, 95% CI = 47.3–53.6). When prescription only forms of paracetamol were included [for example, paracetamol/codeine combinations containing ≥ 30 mg of codeine per tablet (23)], 63% (95% CI = 59.7–65.8) had taken some form of paracetamol in the last week.

The most common form of paracetamol was paracetamol as the only active ingredient (47%, 95% CI = 43.6–49.9; Figure 1). About one-fifth of the sample (22%, 95% CI = 19.3–24.6) had taken some type of paracetamol combination product in the past week, with prescription only paracetamol/codeine combination products [contain ≥ 30 mg of codeine per tablet/unit (23)] the most commonly used paracetamol combination product (17%, 95% CI = 14.4–19.1) used.

The mean daily paracetamol dose in the past week for all paracetamol users in the sample was 2501 mg (SD 1470 mg) and 6.1% of paracetamol users (or 35 participants) had used more than 4000 mg/day on average in the past week (Figure 2). The majority of participants who used paracetamol in the past week used an average of 3000 mg or less per day, with just under one-third of participants taking between 3001 and 4000 mg/day on average in the past week (31%, 95% CI = 27.5–35.0).

Forty-six participants (4.8%, 95% CI = 3.6–6.3) had taken greater than 4000 mg of paracetamol on at least 1 day in the last week and accounted for 8.0% of all paracetamol users (95% CI = 6.1–10.6). Within this group doses ranged from 0 mg to 9540 mg on any day in the last week, however, twenty-four (52.0%, 95% CI = 38.1–65.9) of the forty-six participants had taken more than 4000 mg of paracetamol every day in the last week. The mean daily dose of paracetamol for those who had taken greater than 4000 mg on any day in the last week was 4616 mg (SD 1396 mg).

Participants who had taken greater than 4000 mg on any day in the last week were compared with those who had taken paracetamol in the last week but did not exceed 4000 mg on any day (Table 3). Variables with a p-value less than 0.25 in the bivariate analysis as well as sex were included in the
multivariate binomial logistic regression model (age, income, mean pain severity, pain interference, relief from medications, paracetamol/opioid medication use, opioid dose, depression and pain self-efficacy). Income, paracetamol/opioid combination product use and higher opioid dose were significantly associated with paracetamol use above 4000 mg on any day in the last week. The model was statistically significant (\(v^2 = 25.98, \text{df} = 10, p = 0.004\)) and explained 11% (Nagelkerke R2) of the variance in paracetamol use above the recommended maximum daily dose. The model correctly classified 92.3% of cases, the sensitivity was 2.3% and the specificity was 100%, the positive predictive value was 100% and the negative predictive value was 92.2%. Participants with current income below $399/week had half the odds (Adjusted OR = 0.52, 95% CI = 0.27–0.99) compared to those with higher income of taking greater than 4000 mg of paracetamol on any day in the last week. Participants taking a paracetamol/opioid combination analgesics had twice the odds (Adjusted OR = 2.01, 95% CI = 1.02–4.00) compared to those who did not use combination analgesics of taking greater than 4000 mg of paracetamol on any day in the last week. Total opioid dose was also statistically significant in the multivariate model; however, the odds was only 1.003 (rounded to 1.00, 95% CI = 1.00–1.01). A linearity assumption test confirmed that total opioid dose (as well as all the other

Continuous variables in the model) is linearly related to paracetamol use above 4000 mg on any day in the past week. A graph of the log odds was also plotted against the range of total opioid dose (Figure 3). The graph illustrates that the log odds is linearly related and that the odds ratio is small because of a unit increase over the range of the continuous variable. The odds at the highest total opioid dose (800 mg/ day) in the sample increases to 2.4. Participants taking greater than 4000 mg of paracetamol on any day in the last week were more likely to have a higher total opioid dose.

Discussion

This is the first Australian study to examine use of paracetamol (acetaminophen) among a community sample of people with chronic non-cancer pain. The majority of participants had taken paracetamol in the last week and the most common paracetamol product used contained paracetamol as the only active ingredient, followed by prescription only paracetamol/codeine combination products. A minority had taken greater than 4000 mg on any day in the last week. Those exceeding the recommended maximum daily dose of paracetamol were more likely to have
an income greater than $399/week, to have taken paracetamol/opioid combination analgesics and to be taking a higher dose of opioids.

The reported prevalence of paracetamol and non-opioid medication use above the recommended maximum daily dose varies in the literature from 3.4% to 14% (19,21,39), presumably as a result of different sampling frames and differing use of paracetamol/opioid combination products available in different countries (for example, paracetamol/hydrocodone is not available in Australia but is in the USA). Two US studies (19,39) reported the prevalence of paracetamol use above the recommended maximum daily dose (4.5% and 3.4%), whereas, a Belgian study (21) reported the prevalence of all medication use above recommended maximum daily doses (14%) in a cohort of people with CNCP. One of the US studies (19) examined paracetamol users whereas the other two studies (21,39) examined CNCP samples, however, the study on paracetamol users reported an association with CNCP. Although there are differences in the samples used in the literature and this study, they all identify a small group of people who use paracetamol or non-opioid medications above recommended maximum daily doses for CNCP.

The association between use of paracetamol above the recommended maximum daily dose and use of paracetamol/opioid combination analgesics, appears to support previous studies that reported about one-fifth of people who receive prescribed paracetamol/opioid combination products are exceeding 4000 mg paracetamol per day (13). However, unlike the US studies, we do not know whether the scripts people were given exceeded 4000 mg/day or whether they took additional OTC paracetamol or extra prescribed paracetamol products to increase the daily dose above 4000 mg (13,18). While, the results of this study seem to support the FDA’s decision to decrease the dose in paracetamol/opioid combination products it must be stated that a 325 mg dose of paracetamol is sub-therapeutic and by using paracetamol and opioids separately, the doses can be titrated to an individual’s pain response.

The association between use of paracetamol above the recommended maximum daily dose and higher total opioid dose although statistically significant in the multivariate model, did not appear to be clinically significant. However, the plot of the log odds demonstrated the unit increase associated with total opioid dose. This means that a single unit increase in total opioid dose (1 mg) does not have a clinically meaningful effect, however, a large increase does. The association between total opioid dose and paracetamol use above the recommended maximum daily dose is consistent with other study findings (13,15,21). This suggests that people who use paracetamol above the recommended maximum daily dose may be more reliant on medications to relieve their pain. Studies have reported that the majority of participants, who had used above the recommended maximum daily dose of paracetamol, did so to achieve adequate pain relief (40,41) and reviews on the effectiveness of opioid medications report only a modest level of pain relief (5–7). The association with higher opioid dose and paracetamol use above the recommended maximum daily dose suggests that there are a group of patients for which medications may not provide sufficient pain relief, and for whom other non-medication based treatments may be particularly important.

This study is the first to find an association between use of paracetamol above the recommended maximum daily dose and income. This finding could be explained by differences in the healthcare system in Australia. The Australian healthcare system publicly subsidises prescriptions for some OTC-strength analgesic medications (including some paracetamol products) to people who suffer from...
chronic arthropathies (34) or if they have a healthcare card (given to low income earners who receive a government pension) (42). The cut-off for income used in this study (i.e., less than AUS$399/week) is approximately comparable with the income from unemployment or disability benefits. As a result, it is likely that there are more healthcare card holders among the lower income group, and medical practitioners and pharmacists may supervise paracetamol use more closely among this group. Unlike other studies (15,30), we did not find an association with smoking status at bivariate level, possibly because of a low smoking prevalence in Australia compared with that observed in different countries (33).

This is the first Australian study of its scale to provide a context for paracetamol use in people living in the community with CNCP, reporting on a 1 week snapshot of medication use. As such, we do not know if the observed patterns are typical of paracetamol and opioid use over a longer time period. As the study has no measure of liver function, we also cannot comment on outcomes (such as hepatotoxicity) that may be important in better understanding adverse effects that may be associated with higher than recommended doses of paracetamol. However, a previous study in the USA on paracetamol/opioid combination prescriptions exceeding 4000 mg/day have indicated that a small proportion (n = 3818, 0.1%) of users developed liver dysfunction in the study period. Although this number is small, those who had a script exceeding 4000 mg/day of paracetamol accounted for 23% (n = 894) of the sub-sample with liver dysfunction (13). In addition, it is possible that some participants were reluctant to disclose paracetamol use or daily dose; however, paracetamol use is not stigmatised like adherence to opioid treatment and all participants were informed that the interviews were confidential, de-identified and that their responses would not affect their medical treatment. Self-report of medication dose is subject to the possibility of recall bias (43); however, this is unlikely as participants were sent the diary before the interview and previous research on the topic has reported low rates of over reporting (1%) (44). In addition, self-report data are the best available data for this current study as patients’ prescribing records would not capture over the counter and/ or PRN medication use. The POINT study is a longitudinal study and in the future it may be possible to examine paracetamol use over a 24-month period and link use to adverse outcomes in linked data sets for the cohort.

This study identified that a large proportion of people with CNCP prescribed opioids, use paracetamol (63%). Paracetamol as the only active ingredient was the most commonly used form of paracetamol (47%), followed by paracetamol/ codeine combination products (22%). While the majority of paracetamol users used less than 3000 mg of paracetamol per day, this study also identified a small group of people that were using paracetamol above the recommended maximum daily dose (4.8% of the sample or 8.0% or paracetamol users, used >4000 mg on at least 1 day in the past week). Those who had taken paracetamol above the recommended maximum daily dose were less likely to have a low income, more likely to have a higher total opioid dose and more likely to use a paracetamol/opioid combination analgesic. These findings have important clinical implications, namely that health professionals should actively question paracetamol use in people with CNCP prescribed opioids, particularly if they perceive their medication regime to be inadequate or use a paracetamol/opioid combination analgesic.

Acknowledgements

We thank Gabrielle Campbell, Jessica Belcher, Sarah Freckleton, Anika Martin, Ranira Moodley, Kimberley Smith and Rachel Urquhart-Secord, NDARC, for their contribution to data collection. We also thank Cerissa Papanastasiou, Burnet Institute, for her contribution to some of the POINT data collection in Melbourne. We thank the Pharmacy Guild of Australia, the NSW Pharmacy Guild and Pain Australia, for their support of this study and assistance with dissemination. We also thank the POINT advisory committee for their advice on the design and conduct of the study.

This study received funding from the Australian National Health and Medical Research Council (NHMRC, #1022522). L.D., B.L., S.N., N.G. and W.H. are supported by NHMRC research fellowships (#1041472, #1073858, #1013803, #569738, #1091878 and #1045318). The National Drug and Alcohol Research Centre at the University of NSW was supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grant Fund. Cerissa Papanastasiou was supported by funding provided to Paul Dietze and L.D. by the Victorian Drug Law Enforcement Fund.

Principal Investigator: Louisa Degenhardt.

Authors’ contributions

B.H., L.D., B.L., S.N. and N.G. led writing for the first draft. All authors contributed to the critical review of the manuscript. L.D., R.B., N.L., M.F., M.C., W.H., B.L., S.N. and F.S. contributed to the development of the study for the purposes of the funding proposal and development of the study design.

References


16 FDA recommends health care professionals discontinue prescribing and dispensing prescription combination drug products with more than 325 mg of acetaminophen to protect consumers [Internet].


17 FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure, 2011.


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Int J Clin Practice, 69, 1366-76. 10.1111/ijcp.12716. Please refer to published version for tables mentioned in the text.


