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PAIN

Examination of the clinical factors associated with attendance at emergency departments for chronic pain management and the cost of treatment relative to that of other significant medical conditions

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ABSTRACT

1
2 Little is known about risk factors for emergency department (ED) attendance for
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4 chronic pain (CP) management and the relative service burden. We examined emergency
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6 department (ED) utilisation in patients with chronic pain (CP), identified risk factors
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8 associated with attendance for chronic musculoskeletal pain (CMP) and estimated the
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10 comparative cost of treatment. The study cohort comprised a random sample of 3,700 adults
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12 from the general population in Tayside, Scotland. Linked regional extracts, spanning a 12-
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14 month period, were obtained from national registers, providing information on ED
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16 attendances, community-dispensed prescribing and outpatient clinic attendances. The NHS
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18 Scotland Cost Book was used to ascertain the current average cost of an ED attendance
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20 (£130; ~\$167).
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26 All-cause ED attendance was higher in those with CP (68.5%; n=252) than without
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28 (29.3%; n=967). In the entire cohort, more patients attended the ED for the treatment of
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30 CMP than for any other medical condition (n=119; 32.3% of those with CP). Risk factors for
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32 ED attendance for CMP were: recent analgesic dose decreases (OR=4.55); and transitioning
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34 from opioid to non-opioid analgesics (OR=5.08). Characteristics protective of ED attendance
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36 for CMP were: being in receipt of strong opioids (OR=0.21); transitioning from non-opioid to
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38 opioid analgesics (OR=0.25); recent analgesic dose increases (OR=0.24); and being
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40 prescribed tricyclic antidepressants (OR=0.10), benzodiazepines (OR=0.46) or hypnotics
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42 (OR=0.45). CMP was one of the most expensive conditions to treat (£17,680 (~\$22,668) per
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44 annum), conferring a substantial burden on ED services. Improved understanding of the
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46 risk/protective factors could inform healthcare redesign to reduce avoidable ED attendances
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48 for CMP management.
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Full title: Examination of the clinical factors associated with attendance at emergency departments for chronic pain management and the cost of treatment relative to that of other significant medical conditions

Running head: Chronic pain in emergency departments

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Examination of the clinical factors associated with attendance at emergency departments for chronic pain management and the cost of treatment relative to that of other significant medical conditions

INTRODUCTION

Emergency departments (EDs) internationally are under constant pressure to meet increasing demand [711,2131,2434,2738,2839,3449,3752]. A proportion of patients may represent potentially avoidable demand, such as some of those attending for chronic pain (CP) management. Indeed, many ED attendances for chronic diseases are reported to be preventable [5979]. Furthermore, the ED is not considered to be an appropriate setting for the management of CP [24,5270,6181,6282], and ED staff feel undertrained in treating this problem [85]. In order to better manage health services and treat patients more effectively, it is important to quantify the scale of this issue and understand the risk factors associated with ED attendance for the management of CP.

CP is defined as pain that persists beyond that of normal tissue healing time, usually considered to be 3 months [2940]. A systematic review of UK prevalence studies of CP [4625] reported a pooled prevalence estimate of 43.5% (95% CI 38.4% - 48.6%). CP ‘flare-ups’ are common, reported to occur in up to three quarters of patients with chronic non-cancer pain (CNCP) [4462]. CP accounts for 10-16% of all ED attendances in the USA [36,5270] with some individuals being heavily reliant on emergency service resources [5371,6181]. However, comparative UK figures are not currently available. Effective community-based pain management, with continuity of care, may help to reduce the pressure on emergency services whilst providing more stable pain management for patients. Indeed, a number of systematic reviews have reported the effectiveness of self-management techniques [4116], community-based strategies [3853] and work-based interventions [4158].

Very few studies have examined ED attendance for the management of CP. The precise nature of data collection in EDs in Scotland does not currently allow identification of all patients attending for CP management. Surrogate measures may potentially be used, such as recording of attendance for painful musculoskeletal conditions (excluding injury) among those identified with CP. The Global Burden of Disease (GBD) 2017 Study showed that painful musculoskeletal conditions are the highest contributor to global disability and that low back pain has remained the single leading cause of disability since the first GBD Study in 1990 [2333]. Indeed, one in two adult Americans are reported to live with a painful musculoskeletal condition, a prevalence comparable to that of cardiovascular and chronic respiratory diseases combined, totalling a cost of \$213 billion in 2011, or 1.4% of gross domestic product [5472]. Painful musculoskeletal conditions are reported to consume almost a tenth of the UK's National Health Service (NHS) budget, making this one of the most expensive specialties, after psychiatric disorders and cardiac disease [4563]. The present study aimed to:

- 1) Quantify the proportion of those identified with CP who attended the ED for any reason within a 12-month period and, specifically, those who attended for the treatment of CMP;
- 2) Characterise prescribed analgesic treatment in those identified with CP who attended the ED for any reason compared with those with chronic pain who did not attend the ED;
- 3) Identify the clinical factors associated with ED attendance for CMP;
- 4) Estimate ED resource utilisation associated with CP management compared with other significant medical conditions.

METHODS

Participants and setting

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The study cohort comprised a random sample of 3,700 adults from the general population in the NHS Tayside Health Board area, drawn from the 2014 database of all individuals registered with a general practitioner (GP) in NHS Tayside. Each individual registered with a GP (>95% of the UK population) is assigned an NHS Community Health Index (CHI) number, a unique personal identifier that is contained within the medical records associated with all NHS events. This identifier was used to achieve record linkage and pseudo-anonymisation, as described below. The sample was generated by Health Informatics Centre (HIC) Services, Farr Institute, University of Dundee, using algorithms based on random number generation. All Scottish NHS services, including general practitioner services, are delivered free at the point of contact to all patients, and this includes the dispensing of prescribed medication.

Data sources

Regional data extracts were obtained from several national Scottish health registers, which are held by the Information Services Division (ISD) of National Services Scotland (NSS) and were accessed by HIC Services. The Accident & Emergency Datamart provides a record of all ED attendances and contains information on admission, diagnoses, treatment and discharge. The Prescribing Information System (PIS) is a dataset that contains information on the drugs, dosages and instructions for all community-dispensed prescriptions. The Scottish Morbidity Register (SMR) 00 contains a record of all NHS outpatient clinic attendances by specialty. The SMR06 is a register of all patients diagnosed with malignant disease. Demographic data were provided by HIC Services, from the NHS CHI dataset. These data comprised: gender; age; socioeconomic status using the Scottish Index of Multiple Deprivation (SIMD) quintiles (<https://www.gov.scot/collections/scottish-index-of-multiple-deprivation-2020/>); and urban-rural habitation using the Scottish Executive Urban Rural

1 Classification (SEUR; [https://www.gov.scot/publications/scottish-executive-urban-rural-
3 classification-2005-2006/pages/8/](https://www.gov.scot/publications/scottish-executive-urban-rural-
2 classification-2005-2006/pages/8/)). In accordance with SIMD recommendations, quintiles 1-
4 2 were used to indicate relative socioeconomic deprivation and quintiles 3-5 were used to
5 indicate relative socioeconomic affluence. Scottish Health Service Costs (commonly referred
6 to as the ‘Cost Book’) was used to ascertain the average cost of each ED attendance, which
7 falls at £130 (~\$167). [This unit cost is consistent with the unit cost used in previous UK-
8 based studies, accounting for inflation \[14,21,24,26,59\]](#). Whilst the data used in the present
9 study were collected in 2014, most recently-published Cost Book prices were used in
10 calculating ED costs for each participant to allow a current understanding of the findings
11 presented here. The most recent Cost Book (2017) for each specialty can be found at
12 <http://www.isdscotland.org/Health-Topics/Finance/Costs/A-Z-Index/>, where ED costs by
13 health board can be found in Table R044X.
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31 ***Procedure***

32 Data were extracted from each of the datasets spanning a 12-month period for each
33 participant (i.e. the 2014 calendar year). All data were linked electronically within a secure
34 virtual environment and anonymised prior to release to the research team via a Scottish
35 Government-certified *Safe Haven* (Health Informatics Centre (HIC) Services, University of
36 Dundee).
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45 We used prescribing records to identify people likely to have chronic pain.
46 Participants were identified as having ‘chronic pain’ if they had been in receipt of
47 prescription analgesics for at least three consecutive months during the observation period.
48 Participants identified as having ‘acute pain’ (receipt of analgesic treatment for less than
49 three consecutive months within the observation period) were excluded from the present
50 study. Within the PIS prescribing dataset there is a fully-completed field containing British
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1 National Formulary (BNF) codes (http://gmmmg.nhs.uk/html/formulary_bnf_chapters.html)
2 used to indicate intention to treat, and these codes were used to identify participants who had
3 been in receipt of analgesic prescriptions. This field was used to ensure that the therapeutic
4 indication was ascertained for medication that could be used for multiple purposes; for
5 example, the use of antidepressants or anticonvulsants in the treatment of pain. Individuals
6 were included in the study where analgesia was indicated as the therapeutic intention for
7 prescribing, and individuals were excluded where the indicated therapeutic intention was
8 other than analgesia. The BNF codes used to identify participants with chronic pain are
9 shown in the supplementary digital content (*Table S1*).

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22 Malignant disease was identified through inclusion within the SMR06 and/or
23 attendance at outpatient palliative care services (SMR00). The presence of opioid
24 dependence was identified using BNF codes in the prescribing dataset (4.10.3 Opioid
25 dependence). BNF codes in the prescribing dataset were also used to identify unipolar mood
26 disorders (4.3 Antidepressant drugs), bipolar disorder (4.2.3 Drugs for mania and
27 hypomania), anxiety disorders (4.1.2 Anxiolytics), sleep disorders (4.1.1 Hypnotics) and
28 psychotic disorders (4.2.1 Antipsychotic drugs and 4.2.2 Antipsychotic depot injections).
29 The receipt of pain treatment in secondary care was identified using the SMR00 (treatment at
30 specialist pain services). However, it is important to note that chronic pain may be managed
31 in other specialist settings (such as rheumatology), but it does indicate the use of secondary
32 care pain services. The data did not permit the identification of non-pharmaceutical
33 interventions for the treatment of pain.

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51 Reasons for attendance at the ED were ascertained using the 'Diagnosis Code' field
52 contained within the ED dataset. These data are recorded, at the time of attendance, as high-
53 level codes, indicating the specialty of the presenting complaint. Data were extracted for
54 some of the main significant clinical conditions: CMP ('12 musculoskeletal, excluding
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1 injury’); cardiovascular disease (’03 cardiovascular’); respiratory disease (’17 respiratory’);
2 gastrointestinal disorders (’08 gastrointestinal’); endocrine/metabolic disorders (’06
3 endocrine/metabolic’); substance use disorder (’02 alcohol and/or substance use problems’);
4 and psychiatric disorders (’16 psychiatry’). There was no diagnostic code that would cover
5 all chronic pain.
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11 Equianalgesic computations were made only for opioid medication. Morphine-
12 equivalent doses were established using an online equianalgesic calculator based on the
13 American Pain Society guidelines and critical review papers focusing on the issue of
14 equianalgesic dosing (<http://clincalc.com/opioids/>). The morphine-equivalent dose for each
15 of the opioid medications from the present study is reported in the supplementary digital
16 content (*Tables S2 and S3*).
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26 ‘Strong’ and ‘weak’ opioids were identified using the Analgesic Ladder compiled by
27 the World Health Organization (WHO). Overall dose increases and decreases were identified
28 by calculating each participant’s mean dose during the first 3 months of the 12-month
29 observation period and comparing that value with the mean of the final 9 months. A
30 transition from opioid to non-opioid analgesics, and vice versa, was indicated where the
31 cessation or initiation of opioid analgesic treatment occurred at any point during the
32 observation period. No participants transitioned twice during this time, so the groups were
33 mutually exclusive.
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45 The data were hosted, linked and pseudo-anonymised within HIC Services. Since
46 each of the datasets included in the present study comprised data pertaining to NHS events,
47 all datasets included NHS CHI numbers for all individuals present in these datasets. HIC
48 Services used the CHI numbers from the study sample (obtained from the CHI dataset) to
49 identify all relevant individuals and extract all relevant data from the health datasets included
50 in the present study. ~~Data were linked for each participant using the NHS CHI number.~~
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Following linkage and the extraction of all relevant data, CHI numbers were replaced by proxy CHI (proCHI) numbers in the final release, with the key being retained securely within HIC Services. The research team was then able to track events for individuals across all data extracts using the pseudo-anonymised proCHI identifier. Data were analysed within the HIC Safe Haven, which was accessed via a secure web link, and outputs were scrutinised to ensure data security prior to release to the research team.

Statistical considerations

Data were analysed using the Statistical Package for Social Sciences (SPSS; v22). The chi square test was used in the analysis of categorical dependent variables by categorical independent variables. Statistical findings were reported as chi-square value and degrees of freedom ($\chi^2(df)$), probability value (p) and effect size, Pearson's Phi or Cramer's V (ω). Pearson's Phi was used to assess the effect size in 2x2 contingency tables and Cramer's V was used where there were more than two levels in independent variables. Descriptive summary data were presented as number of participants (n) and percentage of group (%).

Univariate analysis of variance (ANOVA) was used to assess continuous dependent variables by categorical independent variables. Statistical findings of the univariate ANOVA were reported as F value, between-subjects degrees of freedom and within-subjects degrees of freedom (F(between-subjects df, within-subjects df)), probability value (p) and effect size, partial eta squared (η_p^2). Descriptive summary data were presented as mean value (\bar{x}) and standard deviation around the mean (σ).

Binary logistic regression was used to assess the independent predictive capacity of categorical and continuous predictor variables on binary target variables. Tables show unadjusted odds ratio (OR), adjusted odds ratio (OR^{adj}), and 95% confidence interval (95% CI).

Ethical approval

Ethical approval was not specifically required for the present study, since all data were pseudo-anonymised and accessed via a national Safe Haven; however, a favourable ethical opinion was obtained from the East of Scotland Research Ethics Committee (EoSREC) and granted to HIC Services for the curation and linkage of datasets such as these (reference: 14/ES/0015).

RESULTS

An examination of the study population revealed that there was a higher proportion of males (73%, n=2668) than females (27%, n=996). *Figure 1* shows the distribution of age and deprivation status in the study population compared with the general population of Scotland.

[Insert Figure 1 around here]

Figure 1a shows that there was a higher proportion of those aged 30-49 years in the study cohort compared with the general population of Scotland. Consequently, there were lower proportions of those aged 20-29 years and 60+ years. *Figure 1b* shows that there was a higher proportion of deprived (quintiles 1-2) individuals and a lower proportion of affluent (quintiles 3-5) individuals than would be found in the general population.

A breakdown of the numbers in each group having attended the ED during the 12-month observation period is shown in *Figure 2*. This includes attendance by patients with chronic, painful conditions (as defined by analgesic prescribing) and those with chronic pain attending specifically for the treatment of CMP (identified by attendance code).

[Insert Figure 2 around here]

Figure 2 shows that, of the 368 participants identified as having chronic pain, 68.5% (n=252) had attended the ED for any reason on at least one occasion during the observation period, and 32.3% (n=119) had attended for CMP management. *Figure 3* shows the proportion of those with and without chronic pain who attended the ED for any reason on at least one occasion during the observation period, and it describes presenting complaint in those with chronic pain who attended the ED.

[Insert Figure 3 around here]

Figure 3a shows that, compared with those with no pain, a significantly higher proportion of those with chronic pain attended the ED for any reason on at least one occasion during the observation period ($\chi^2(1)=219$; $p<0.001$; $\omega=0.244$). *Figure 3b* shows that almost half of those with chronic pain who attended the ED attended for CMP management. A further 28 participants with chronic pain attended the cardiovascular and gastrointestinal specialties: these participants could have been seeking treatment for chronic pain but there was insufficient clinical information contained within the dataset to determine specific reasons for attendance. *Figure 4* shows analgesic prescribing characteristics in those with chronic pain who did and did not attend the ED during the observation period.

[Insert Figure 4 around here]

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Figure 4 shows that around a quarter of those in receipt of prescribed analgesics were prescribed opioids, and there was little difference in this pattern between groups. There was no group difference in mean oral morphine-equivalent daily dose (oMEDD) between those that attended and did not attend the ED. Analgesic prescriptions were issued for a mean duration of around 6 months during the observation period, and there was little difference between groups. It should be noted that this figure refers to the issue of analgesic prescriptions during the 12-month observation period, and that data were not available to facilitate estimates of the length of time in receipt of analgesic prescriptions outside of the observation period.

Risk of emergency department attendance for chronic musculoskeletal pain management

Table 1 shows the sociodemographic characteristics, analgesic treatment characteristics and medical and psychiatric morbidities associated with risk of attendance at the ED for CMP management. Only 3.0% (n=7) of participants were diagnosed with malignant disease and 1.3% (n=3) had their pain problems treated in a specialist pain service. Due to low numbers, these variables were not included in the analyses.

[Insert Table 1 around here]

Table 1 shows that a significantly higher proportion of those that attended for the treatment of CMP was male and relatively socioeconomically affluent. In consequence, the remainder of the analyses were adjusted for gender and deprivation status. The adjusted odds ratios show that being prescribed strong opioids, transitioning from non-opioid to opioid analgesics and recent analgesic dose increases were each independently protective of ED attendance for CMP management. Conversely, recent analgesic dose decreases and

1 transitioning from opioid to non-opioid analgesics were predictive of ED attendance in this
 2 group. Furthermore, there were no associations with medical morbidity, but being in receipt
 3 of prescribed antidepressants (specifically tricyclics), benzodiazepines and hypnotics for the
 4 treatment of psychiatric disorders were independently protective of ED attendance for CMP
 5 management.
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11 *Relative cost of emergency department treatment for chronic pain management*

12 All ED attendances (n=1,219) were included in calculating the cost of ED treatment
 13 for CMP relative to that of other clinically-significant morbidities. This included participants
 14 with chronic pain (n=252) and without chronic pain (n=967). Findings are shown in *Table 2*.
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27 [Insert Table 2 around here]

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 31 *Table 2* shows that more patients attended the ED for the treatment of CMP than for
 32 any other clinically-significant medical condition, and that this was one of the most expensive
 33 conditions overall to treat, second only to that of cardiovascular disease. Based on a Scottish
 34 population estimate of 5.42 million and the figures in the present study, more than 174,000
 35 patients are likely to seek treatment for CMP management across Scotland in any 12-month
 36 period, with ED costs for the treatment of this condition likely to amount to around £26
 37 million (~\$33 million).
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51 **DISCUSSION**

52 More than two thirds of those identified with CP attended the ED for any problem
 53 during the observation period, with almost a half of these attending for CMP management. A
 54 higher proportion of those that attended with CMP was male and relatively
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1 socioeconomically affluent. Being in receipt of prescribed strong opioid analgesics,
2 transitioning from non-opioid to opioid analgesics and recent analgesic dose increases were
3 each independently protective of ED attendance for CMP management. Conversely, recent
4 analgesic dose decreases and transitioning from opioid to non-opioid analgesics were
5 predictive of ED attendance. Being in receipt of prescribed tricyclic antidepressants,
6 benzodiazepines and hypnotics were independently protective of ED attendance for CMP
7 management. More patients attended the ED with CMP than with any other medical
8 condition, and this was one of the most expensive conditions overall to treat. Projected
9 estimates suggest that almost 175,000 patients are likely to seek treatment for CMP across
10 Scotland (population = 5.42M million) in any 12-month period, with ED costs for the
11 treatment of this condition likely to amount to around £26 million (~\$33 million).

26 As a result of data collection processes across Scottish EDs, it is not currently
27 possible to identify all attendances for CP management. As discussed, the present study used
28 the best available surrogate indicator – painful musculoskeletal conditions (excluding injury);
29 however, this fails to encompass important conditions, such as abdominal and pelvic pain,
30 and some presentations may have been for relatively short-term problems (although in people
31 already identified with CP). In an examination of all loci of pain in 5,279 patients with CP in
32 the UK [913], 7443 specific sites of pain were reported. Most loci were suggestive of
33 musculoskeletal pain (89%); however, there was also a substantial prevalence of abdominal
34 (8%) and pelvic (3%) pain. In consequence, the prevalence and costs reported in this article
35 are likely to be an underestimate of the true burden of CP placed upon ED resources.

51 ~~Whilst CP is more prevalent in females than males [8,17,26,48,55,57], the present~~
52 ~~study found that male gender was a risk factor for ED attendance for CMP. A higher~~
53 ~~prevalence of chronic pain is often reported in females [12,27,37,66,73,75], and females are~~
54 ~~associated with more frequent ED attendance [5,55]. However, similar to the findings of a~~

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previous study examining all-cause ED attendance [2], the present study found that male gender was a significant risk factor for ED attendance for unmanageable pain. Men are reported to be twice as likely as women to have inadequate health literacy [76]. Furthermore, men have been shown to be less likely to seek medical assistance from general practitioners [1,23,35,78], pharmacists [56] and pain services specifically [10,22,45] when they are ill. It may be the case that men are relatively reluctant to seek medical assistance prior to reaching crisis stage; indeed, Juel and Christensen [43] suggested a link between men's lower use of primary care and higher use of hospital services in their analysis of 35.8 million general practitioner attendances and 1.2 million hospitalisations in Denmark during 2005. Our data, however, do not allow a definitive explanation for this finding. All-cause ED attendance is reported to be most common in socioeconomically deprived individuals [6,31,49]. However, similar to the findings of Poulin and colleagues [46], the present study found that socioeconomic affluence was a risk factor for ED attendance specifically for CMP management. A higher proportion of males and affluent individuals may be more likely to be in full-time employment thus finding it harder to attend a GP practice during working hours; indeed, Zhou and colleagues [64] found that the inability to get to an in-hours GP appointment was associated with higher use of out-of-hours healthcare services. ED attendance for any complaint is reported to be most common in socioeconomically deprived individuals [9,46,67], and these individuals have been shown to demonstrate a preference for hospital treatment compared with primary care [44]. However, similar to the findings of Poulin and colleagues [64], the present study found that relative socioeconomic affluence was a risk factor for ED attendance specifically for acute exacerbation of chronic pain. Joynt and colleagues [42] found that patients from the highest socioeconomic quartile were more likely to receive opioid analgesics on presentation at EDs compared with those from the lowest quartile, and it may be that a proportion of those with low socioeconomic status avoid the ED

based on previous experience of not having received immediate pain relief. However, it is impossible to interpret this finding without further research.

Whilst prescription opioids are associated with increased overdose risk [4217,5674,6080] and high doses are associated with ED attendance for alcohol- and drug-related problems [47], the present study found that opioid (compared with non-opioid) analgesics and higher doses were protective of ED attendance for CMP management. Furthermore, recent opioid analgesic dose reductions and transitioning from opioid to non-opioid analgesics were risk factors for ED presentation with CMP. An understanding of the potential adverse effects of opioid tapering in patients with CP is yet to be achieved, as highlighted in a recent systematic review of the topic [3550]. However, one study [3651] found that, following analgesic opioid tapering and eventual discontinuation in patients with CNCP, 49% of their 494 participants experienced an opioid-related hospitalisation or ED attendance as a result of overdose or other problems associated with problematic use. As with our present study, these findings echo a recent Food and Drug Administration (FDA) safety announcement concerning potential ‘serious harm’ associated with rapid tapering or discontinuation of opioid analgesics, such as withdrawal symptoms, uncontrolled pain, psychological distress and suicide [2232]. Whilst there are potential risks associated with opioid prescribing, the findings of this study suggest that adequate pain management may help to stabilise pain problems in patients with CP and reduce the need for ED intervention, and that opioid tapering or discontinuation should not be implemented in the absence of an alternative pain management plan and careful monitoring of potential adverse effects.

Being in receipt of prescribed tricyclic antidepressants (but not selective serotonin reuptake inhibitors (SSRIs)), benzodiazepines and/or hypnotics for the management of psychiatric disorders was independently protective of ED attendance for CMP management. Tricyclic antidepressants (TCAs) and serotonin noradrenaline reuptake inhibitors (SNRIs) are

commonly used in the treatment of chronic neuropathic pain

[4][3,4318,4929,2030,3954,4765]; whereas, SSRIs are ineffective in CP management [4][3,4015,4929,2030]. Furthermore, a recent systematic review of randomized control trials [3348] highlighted the effectiveness of TCAs in treating insomnia. Insomnia is shown to exacerbate pain problems [4828,3247,50], and the potential therapeutic effect of TCAs on insomnia may account for the protective effect on ED attendances for CMP in a portion of patients with CP.

Clinical insomnia and anxiety disorders are more prevalent in individuals with CP than in pain-free controls [4260,5169,5877]. Pain is now widely understood as a multidimensional construct featuring a strong emotional component in addition to sensory experiences [2940], and pain problems are shown to be exacerbated by both anxiety [2536,6383] and insomnia [4828,3247,5068]. Our findings that benzodiazepine or hypnotic use reduced ED attendance for CMP may relate to the central effects of these agents, with a possible decrease in anxiety (or insomnia), although these agents are recommended only for short term use. Furthermore, there are serious risks associated with the concomitant use of opioids and central nervous system depressants, which can ultimately result in premature mortality due to respiratory depression [4419,3041,4057,4361]. There is a need for further studies examining non-pharmaceutical interventions for the treatment of anxiety disorders and insomnia in patients with CMP to ensure safe and effective clinical practice.

To the authors' knowledge, this is the first study to examine the burden that CMP places upon EDs. CMP was the second most resource-intensive medical condition to treat in the ED, despite previous findings suggesting that CP is not most effectively managed by emergency services [24,5270,6181,6282]. Indeed, this finding further supports the proposal that effective community-based pain management could alleviate some of the pressure placed upon EDs, and that there is a need to identify and implement treatments that are at least as

1 effective as analgesic pain management for patients who require opioid tapering. The
2 projected national cost estimates presented here require validation in national studies, and
3
4 further research is required to understand patients' motives for, and expectations of,
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6 presentation at EDs with CMP. Only through the proposed further research can cost-effective
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8 pain management policy be developed which could deliver effective treatment to those with
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10 CMP, thereby improving overall quality of life.
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17 *Limitations*

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19 The study cohort was characterised by a relatively high proportion of males and a
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21 lower proportion of those aged 60+ years compared with the Scottish population as a whole,
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23 and this may have resulted in an underestimation of pain prevalence and treatment costs
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25 [4625]. Conversely, the relatively high proportion of socioeconomically deprived individuals
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27 may have resulted in an overestimation of these figures due to the poorer health associated
28
29 with these socioeconomic groups [4520]. A key limitation of the present study is that the
30
31 identification of participants with CP was based on community-dispensed analgesic
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33 prescribing for at least 3 consecutive months within the observation period; ~~and this,~~
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35 therefore, this did not include individuals who were treated only with non-pharmaceutical
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37 interventions or over-the-counter (OTC) medication, and it may have resulted in the
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39 exclusion of some individuals who had been hospitalised during the observation period or
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41 had migrated to the area relatively recently. In consequence, the findings of the present study
42
43 are likely to be an underestimation of the numbers attending the ED with CP and the total
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45 cost of treatment. The principal limitation in estimating the burden of CP on ED resources is
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47 that, due to the nature of ED data coding, it is not currently possible to identify all
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49 attendances for CP. Attendance for CMP was considered the most appropriate surrogate
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51 indicator. A further limitation is that the Scottish Morbidity Register (SMR) 00 (outpatient
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1 clinic activity) is known to provide underestimates of the number of patients attending
2 specialist pain services, which may account for the insufficient numbers in the present study
3 to enable statistical testing. It should be noted that patients may have their CP treated in other
4 specialist services (such as orthopaedics or neurology) but that administrative datasets do not
5 provide sufficient clinical information to identify these patients. Finally, psychometric
6 assessment of the process of assigning BNF codes (indicating intention to treat) in the
7 prescribing dataset could strengthen research using these data.
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18 **Conclusions**

19 All-cause ED attendance was significantly higher in those with CP compared with
20 those with no evident pain. More patients attended the ED for the treatment of CMP than for
21 any other medical condition, and this was one of the most expensive conditions to treat,
22 second only to cardiovascular disease. We have identified some sociodemographic and
23 treatment-related factors associated with the rates of attendance that need to be considered
24 with circumspection. There is a need to identify effective, community-based, non-
25 pharmacological interventions to ensure safe treatment practices for patients with CMP and to
26 help to reduce the need for ED interventions in the management of this chronic condition.
27 Further research is needed to understand the factors that drive treatment-seeking behaviour,
28 such as ED attendance, for CMP management.
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58 **DATA SHARING STATEMENT**

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1 In accordance with the information governance policies of the data gatekeepers, the data used
2 in the present analyses are not available for sharing.
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Figure legends

Figure 1: a. Distribution of age in the study cohort (percentages) compared with the distribution in the general Scottish population; and b. distribution of Scottish Index of Multiple Deprivation (SIMD) quintiles in the study population compared with the equal distribution (denoted by a horizontal line) found in the general population

Note: Scottish population age group data were obtained from the Office for National Statistics

(<https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationprojections/datasets/tablea26principalprojectionscotlandpopulationinagegroups>)

Figure 2: Breakdown of cohort by presence or absence of chronic pain and attendance at emergency departments

Figure 3: a. Proportions with chronic pain and no pain attending the emergency department for any reason on at least one occasion during the observation period; and b. presenting complaint in those with chronic pain who attended the emergency department

Figure 4: Analgesic prescribing characteristics in those with chronic pain who did and did not attend the emergency department during the observation period (a. percentage of participants in receipt of prescribed opioid analgesics; b. mean oral morphine-equivalent daily dose (mg) per patient over the 12-month observation period of those who were in receipt of prescribed opioid analgesics; c. mean months duration in receipt of any analgesic prescriptions during the observation period)

Summary

Emergency department attendance was higher in those with than without chronic pain. Risk factors for attendance suggest a need to apply more effective non-pharmacological treatments.

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Figure 1

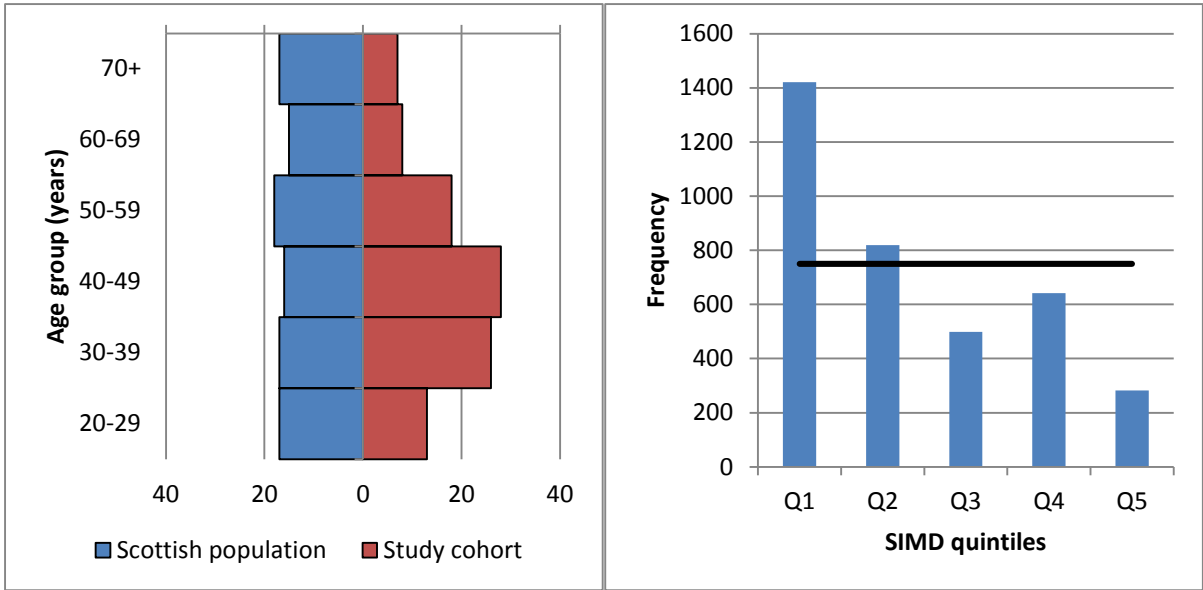


Figure 2

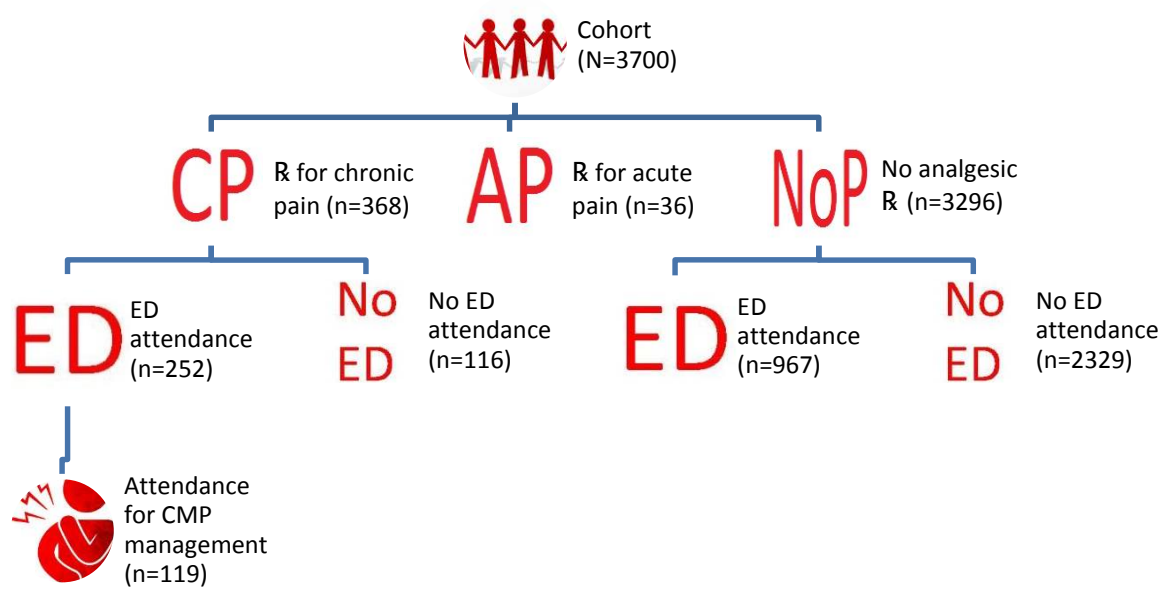


Figure 3

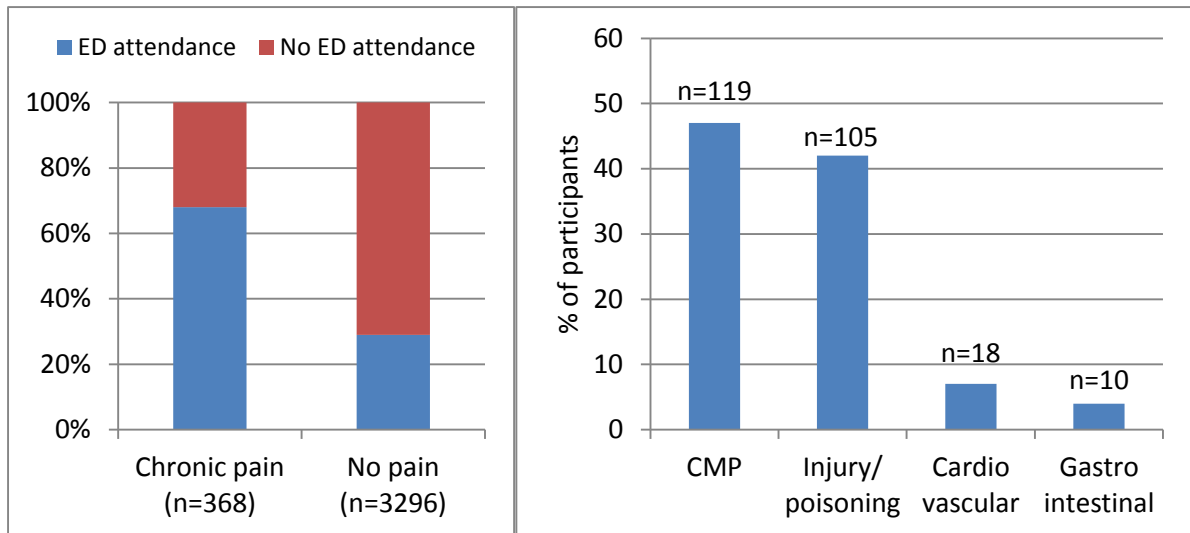


Figure 4

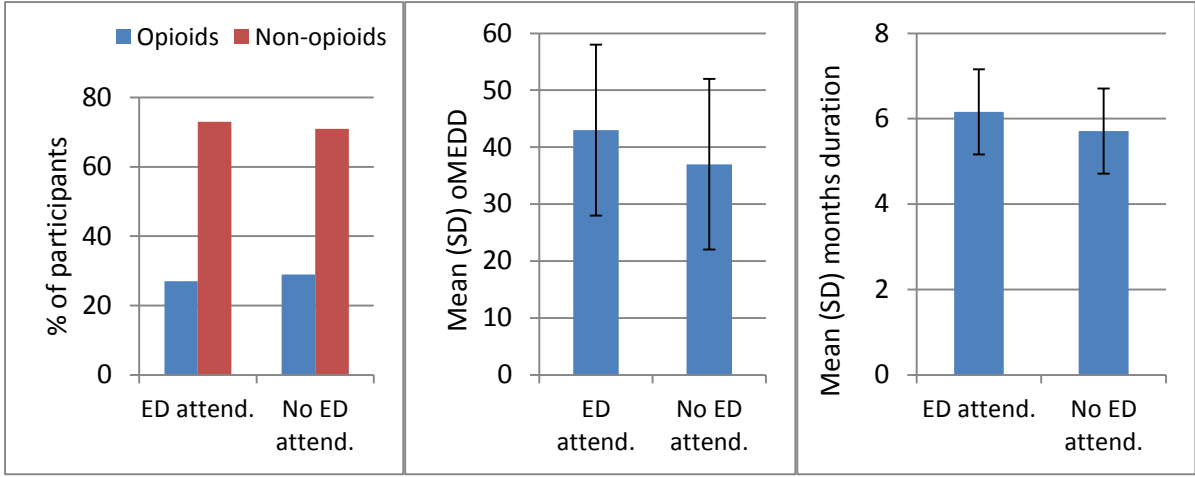


Table 1: Sociodemographic characteristics, analgesic treatment characteristics and psychiatric morbidity in those with chronic pain who attended the emergency department for the treatment of CMP in 2014 (n=119) compared with those with chronic pain who did not attend the emergency department (n=116)

Predictor	Reference	OR	OR ^{adj}	95% CI
<i>Sociodemographic characteristics</i>				
Male	Female	2.21	-----	0.26-3.89
Age	Each 1-year increase	0.99	-----	0.97-1.01
Socioeconomically affluent	Relatively deprived	2.06	-----	1.21-3.51
Rural habitation	Urban habitation	1.76	-----	0.94-3.27
<i>Analgesic treatment characteristics</i>				
Opioid analgesics	Non-opioid analgesic	0.78	0.77	0.38-1.55
Strong opioids	Weak opioids	0.18	0.21	0.05-0.89
Opioid to non-opioid	No change in class	5.39	5.08	1.42-18.16
Non-opioid to opioid	No change in class	0.23	0.25	0.07-0.94
Increase in analgesic dose	No change in dose	0.25	0.24	0.11-0.53
Decrease in analgesic dose	No change in dose	4.50	4.55	1.75-11.83
<i>Treatment for medical morbidity</i>				
Gastrointestinal (GI) disorders	No GI disorders	0.62	0.68	0.35-1.34
Cardiovascular (CV) disease	No CV disease	0.86	1.67	0.85-3.28
Respiratory disorders	No respiratory disorders	0.74	0.86	0.45-1.61
Endocrine disorders	No endocrine disorders	0.58	0.66	0.34-1.26
<i>Treatment for psychiatric morbidity</i>				
Opioid agonist therapy *	No mental illness **	1.36	1.64	0.95-2.85
Antidepressants	No mental illness **	0.39	0.54	0.29-0.99

<i>Tricyclic treatment †</i>	<i>SSRI treatment</i>	0.10	0.10	0.04-0.25
Benzodiazepines ‡	No mental illness **	0.34	0.46	0.21-0.98
Hypnotics	No mental illness **	0.34	0.45	0.20-1.00
Antipsychotics	No mental illness **	0.26	0.36	0.08-1.62

OR^{adj} shows ORs adjusted for gender and deprivation status

* All of these participants were treated with methadone hydrochloride

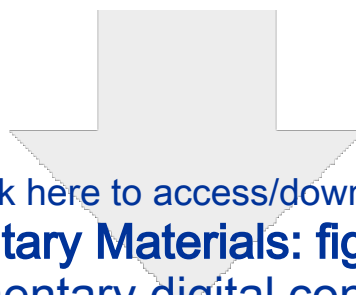
† All participants that were prescribed antidepressant medication were in receipt of either selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs) – no participants were in receipt of monoamine oxidase inhibitors (MAOIs) or other antidepressant medication

‡ All sedatives were included; however, all of these participants were prescribed benzodiazepines, almost exclusively diazepam

** No psychotropic prescribing or attendance at specialist psychiatric services during 2014

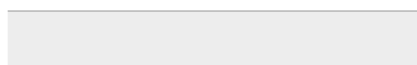
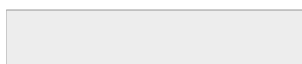
Table 2: Cost of emergency department treatment for clinically-significant medical conditions in the study cohort and estimated national cost based on these figures and a Scottish population estimate of 5.42 million

Medical condition	Study cohort		Scottish population	
	(N=3,700)		(N=5.42 million)	
	n	£cost (\$)	N	£cost (\$)
Cardiovascular disease	100	20,410 (26,168)	146,340	29.87m (38.30m)
Chronic musculoskeletal pain	119	17,680 (22,668)	174,524	25.93m (33.24m)
Respiratory disease	45	12,740 (16,334)	66,124	18.72m (24.00m)
Gastrointestinal disorders	62	12,090 (15,501)	91,056	17.76m (22.77m)
Endocrine/metabolic disorders	25	6,110 (7,834)	36,856	9.01m (11.55m)
Substance use disorder	15	2,080 (2,667)	22,222	3.08m (3.95m)
Psychiatric disorders	14	1,950 (2,500)	20,596	2.87m (3.68m)



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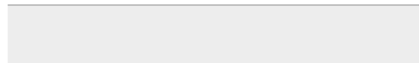
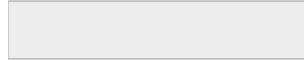
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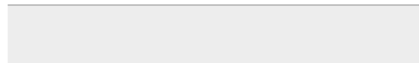
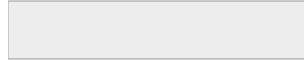
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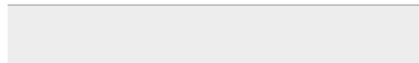
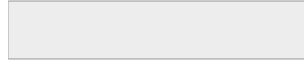
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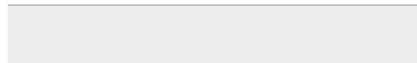
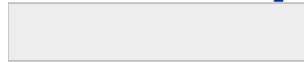
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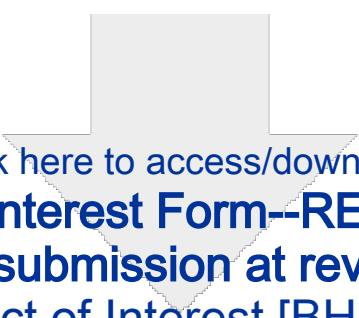




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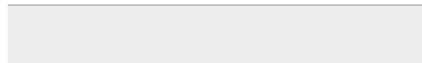
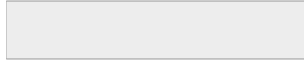
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