

# TREATMENT PATTERNS AND RESOURCE COSTS OF PALLIATIVE CARE FOR ADVANCED CANCER PATIENTS STARTING STRONG OPIOID TREATMENT WITH 12-HOURLY SUSTAINED-RELEASE MORPHINE OR TRANSDERMAL FENTANYL

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## AIM OF INVESTIGATION

This study aimed to quantify resource use and costs of palliative care for advanced cancer patients in the UK from the start of strong opioid treatment with 12-hourly sustained-release (SR) morphine (MST Continus®) or transdermal fentanyl (Durogesic®) until death, from the perspective of the National Health Service (NHS) as well as the voluntary and charitable sector.

## METHODS

- Drug use and resource utilisation by patients with advanced cancer was obtained from the DIN-Link database, which contains longitudinal information on 0.9 million live patients managed by approximately 360 GPs in 100 nationally distributed general practices.
- Patients were included in the data set if they had a Read code for malignant neoplasms and received either 12-hourly SR morphine or transdermal fentanyl as their first strong opioid between 1st January 1998 and 30th September 2000 and died during that period.
- A decision tree modelling palliative care for patients with advanced cancer following initial treatment with 12-hourly SR morphine and transdermal fentanyl was constructed by combining patients' opioid prescribing history with their resource utilisation derived from the DIN-Link database.
- The decision model included the following resource categories obtained from the DIN-Link database: prescribed drugs (i.e. opioids and non-opioids); GP surgery and domiciliary visits; outpatient visits to a palliative care physician; domiciliary visits made by a palliative care physician; and hospitalisation. In addition to these resource categories, specialist nurse domiciliary visits, district nurse domiciliary visits and hospice stay were also quantified.
- Differences in monthly resource use between the treatment groups were tested for statistical significance using a modified 'goodness-of-fit' Chi-Square test, whereby the mean monthly resource use was weighted according to the number of patients in each group.
- The direct healthcare cost of palliative care from the start of treatment until death was estimated by assigning unit costs to the resource utilisation estimates within the decision model.

## CONCLUSION

The total cost of palliative care ranged from a mean £6,709 to £7,720. Because of differences in duration of survival, the monthly cost of palliative care for patients initially treated with 12-hourly SR morphine or transdermal fentanyl alone was a mean £528 and £2,067 respectively. In contrast, the monthly cost of palliative care for patients initially treated with 12-hourly SR morphine or transdermal fentanyl in combination with 4-hourly morphine was a mean £880 and £1,981 respectively.

Less than one-third of all patients also received 4-hourly morphine as part of their initial opioid treatment, despite UK guidelines recommending that the management of moderate-to-severe pain should always start with an immediate-release preparation. Additionally, patients who did receive 4-hourly morphine as part of their initial treatment also received more laxative and anti-emetic prescriptions compared to patients who did not. It also appears that initiation of strong opioid treatment in transdermal fentanyl-treated patients is delayed. These findings suggest that pain in advanced cancer patients is often inadequately managed. Factors such as tumour type, stage of disease, patient's age, opioid side-effect profile, convenience of use and patient preference should inform the decision to choose between opioids with similar analgesic efficacy.

## REFERENCES

- Guest JF, Hart WM & Cookson RF on behalf of the Palliative Care Advisory Committee. Cost analysis of palliative care for terminally ill cancer patients in the UK after switching from weak to strong opioids. *PharmacoEconomics* 1998; 14(3): 285-97.
- Jeal W & Benfield P. Transdermal fentanyl. A review of its pharmacological properties and therapeutic efficacy in pain control. *Drugs* 1997; 53(1): 109-38.
- Ahmedzai S & Brooks D. Transdermal fentanyl versus sustained-release oral morphine in cancer pain: Preference, efficacy and quality of life. *Journal of Pain and Symptom Management* 1997; 13(5) 254-61.
- Billings JA. Recent advances: Palliative care. *British Medical Journal* 2000; 321:555-8.
- Royal College of Physicians. Principles of pain control in palliative care for adults. July 2000.

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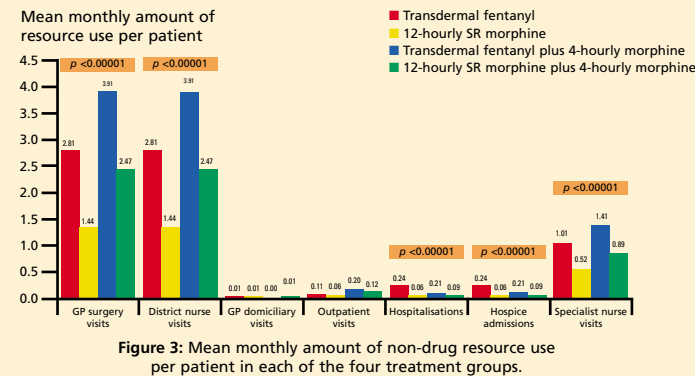
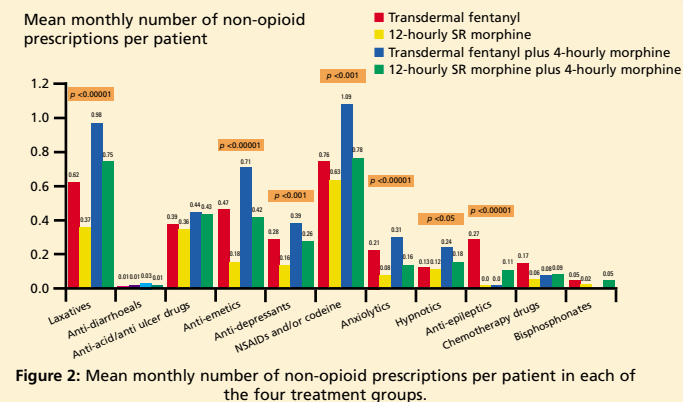
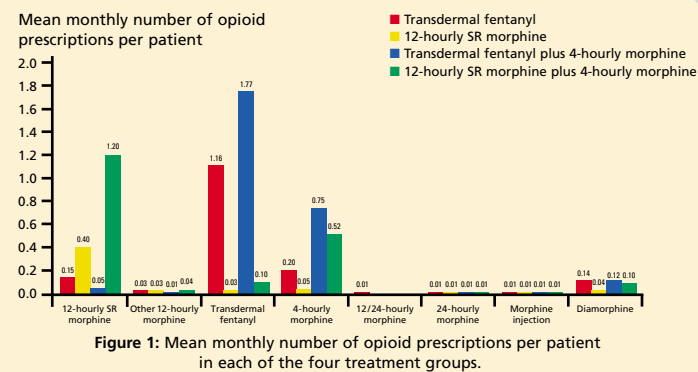
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## RESULTS & DISCUSSION

- The data set contained information on 790 patients who started opioid treatment with 12-hourly SR morphine. Of these:
  - 513 (65%) patients started on 12-hourly SR morphine alone.
  - 271 (34%) patients started on 12-hourly SR morphine plus 4-hourly morphine.
  - 6 (<1%) patients started on 12-hourly SR morphine plus another opioid. Due to the small cohort size, these were not included in the analysis.
- The data set also contained 209 patients who started treatment with transdermal fentanyl. Of these:
  - 153 (73%) patients started on transdermal fentanyl alone.
  - 49 (23%) patients started on transdermal fentanyl plus 4-hourly morphine.
  - 7 (3%) patients started on transdermal fentanyl plus another opioid. Due to the small cohort size, these were not included in the analysis.
- Patients initially treated with transdermal fentanyl with or without 4-hourly morphine received an approximate mean dose of 67mcg and 80mcg fentanyl per hour respectively. Patients initially treated with 12-hourly SR morphine with or without 4-hourly morphine received an approximate mean daily dose of 147mg and 70mg of this opioid respectively.
- Patients' survival and hence treatment duration was:
  - 103 days for patients started on transdermal fentanyl plus 4-hourly morphine.
  - 114 days for patients started on transdermal fentanyl alone.
  - 245 days for patients started on 12-hourly SR morphine plus 4-hourly morphine.
  - 409 days for patients started on 12-hourly SR morphine alone.
- The average period from cancer diagnosis to the start of strong opioid treatment was 8.6 and 6.4 years among patients whose initial treatment included transdermal fentanyl and 12-hourly SR morphine respectively. This equates to an overall period from diagnosis to death of 8.9 and 7.4 years respectively.
- The model showed that 58% and 56% of patients whose initial treatment was 12-hourly SR morphine with and without four hourly morphine respectively remained on this opioid until death. Additionally, 59% and 65% of patients whose initial treatment was transdermal fentanyl with and without four hourly morphine respectively remained on this drug until death. The remaining patients in all four groups underwent several changes in their opioid treatment.

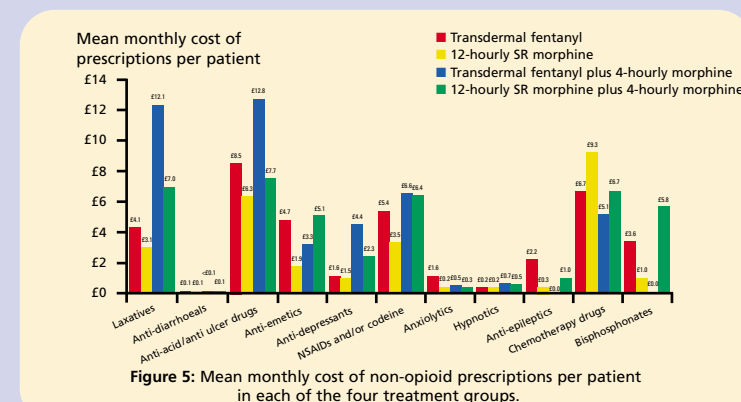
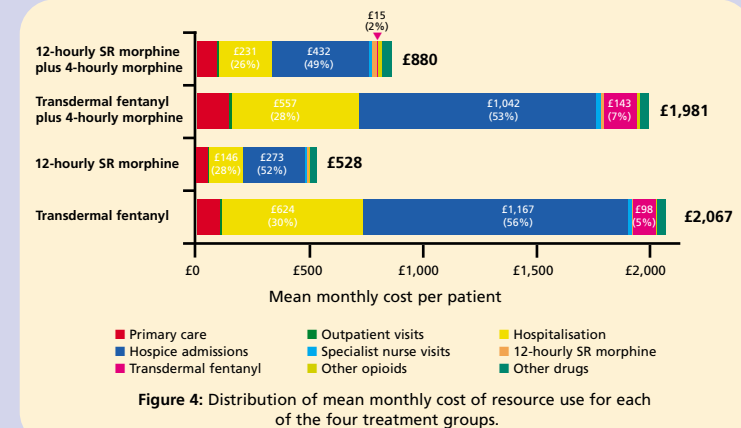
### Resource Use

There were no statistically significant differences between the patients treated with transdermal fentanyl or 12-hourly SR morphine in terms of age and cancer profile. However, statistically significant differences in resource use between the transdermal fentanyl and 12-hourly SR morphine groups were observed for most resource categories (Figures 1, 2 and 3).



### Cost of Resource Use

- The total cost of palliative care was:
  - £2,067 for a patient whose treatment started with transdermal fentanyl alone.
  - £7,103 for a patient whose treatment started with 12-hourly SR morphine alone.
  - £7,084 for a patient whose treatment started with 12-hourly SR morphine plus 4-hourly morphine.
  - £6,709 for a patient whose treatment started with transdermal fentanyl plus 4-hourly morphine.
- The mean monthly cost of palliative care (Figures 4 and 5) was:
  - £2,067 for patients who began treatment with transdermal fentanyl alone.
  - £1,981 for patients who began treatment with transdermal fentanyl plus 4-hourly morphine.
  - £880 for patients who began treatment with 12-hourly SR morphine plus 4-hourly morphine.
  - £528 for patients who started treatment with 12-hourly SR morphine.



- Overall, the mean monthly cost of non-drug resource use was highest among patients who began treatment with transdermal fentanyl, with or without 4-hourly morphine (£1,785 and £1,922 respectively). In contrast, the mean monthly cost of non-drug resource use among patients who began treatment with 12-hourly SR morphine with or without 4-hourly morphine was £780 and £487 respectively.
- The mean monthly NHS cost of palliative care was:
  - £1,265 for patients who began treatment with transdermal fentanyl alone.
  - £1,256 for patients who began treatment with transdermal fentanyl plus 4-hourly morphine.
  - £573 for patients who began treatment with 12-hourly SR morphine plus 4-hourly morphine.
  - £335 for patients who started treatment with 12-hourly SR morphine alone.
 Hence, the NHS incurred almost two-thirds of the cost of palliative care in all groups. The voluntary and charitable sector incurred the remainder.
- Transdermal fentanyl's acquisition cost accounted for 7% and 5% of the total cost of palliative care for patients initially treated with this drug with or without 4-hourly morphine respectively. For patients initially treated with 12-hourly SR morphine with or without 4-hourly morphine, this drug's acquisition cost accounted for 4% and 2% of the total cost of palliative care respectively. Transdermal fentanyl's acquisition cost accounted for 92% to 95% of the mean cost of opioids for patients initially treated with this drug. Patients in the data set were using, on average, one transdermal fentanyl patch every 2 to 3 days in accordance with prescribing guidelines.

### Sensitivity Analyses

- Hospice care was found to be the primary cost driver in the management of patients with advanced cancer and hospitalisation the secondary cost driver.
- The impact on costs of varying the number of primary care visits and specialist nurse visits is negligible.
- Changing the acquisition cost of 12-hourly SR morphine and transdermal fentanyl does not significantly impact on the total cost of palliative care. However, changing the acquisition cost of transdermal fentanyl substantially affects the drug costs associated with palliative care management. For example, a 50% decrease in the acquisition cost of transdermal fentanyl would lead to at least a 34% reduction in monthly drug costs associated with palliative care management in those patients whose initial treatment included transdermal fentanyl. In contrast, a 50% decrease in the acquisition cost of 12-hourly SR morphine would lead to at least a 11% reduction in monthly drug costs in those patients whose initial treatment included 12-hourly SR morphine.

### Discussion

- Patients initially treated with transdermal fentanyl started their strong opioid regime later in their disease progression compared to those patients who started on 12-hourly SR morphine. Furthermore, time to death after starting treatment with transdermal fentanyl was 69% less than that of patients whose initial treatment included 12-hourly SR morphine.
  - The majority of patients initially treated with transdermal fentanyl were treated by GPs who prescribed both opioids. Only 22% of patients initially treated with transdermal fentanyl were managed by GPs who did not also prescribe 12-hourly SR morphine.
  - Patients whose initial treatment included transdermal fentanyl received a mean dose of 76mcg fentanyl per hour. This is equivalent to a morphine dose of approximately 225 to 314mg per day. However, patients whose initial treatment included 12-hourly SR morphine received a mean daily dose of 100mg of this opioid.
- The choice of initial treatment might reflect an individual clinician's perception of prognosis or the stage of the cancer based on defined assessment criteria. Notwithstanding this, patient resistance to the use of morphine and patients delaying strong opioid treatment for as long as possible may also account for these differences, resulting in GPs having to use higher doses of transdermal fentanyl in order to control pain than they would have used had patients started their opioid treatment earlier.
- In a previous cost analysis of palliative care [1], we employed resource use based on information obtained from a Delphi and expert panel, which included opinion leaders. In contrast, this new study is based on naturalistic practice and suggests that constipation is more of a problem among transdermal fentanyl-treated patients than among those who received 12-hourly SR morphine.
- Our present study also found that consumption of anti-diarrhoeal drugs by patients was negligible, irrespective of their initial treatment, whereas clinical studies suggest that transdermal fentanyl-treated patients are more likely to develop diarrhoea than those managed with morphine [2,3]. Hence, diarrhoea is less of a problem in naturalistic practice than clinical trials might suggest.
- Managing patients in the community was found to consume fewer resources than was previously estimated [1]. This present study also estimated that 28% of patients are admitted into hospital, which is broadly consistent with our previous analysis which assumed that 25% of all patients would be admitted into hospital [1]. This suggests that specialists have a greater understanding of patient management in secondary care than in the community.
- Only 34% of patients in the data set who started treatment with 12-hourly SR morphine and 23% of patients initially treated with transdermal fentanyl also received 4-hourly morphine. However, UK guidelines recommend that the management of moderate-to-severe pain should always start with an immediate-release preparation. The findings presented here are consistent with other evidence suggesting that pain is often inadequately managed [4,5]. Additionally, our findings suggest that patients who do receive 4-hourly morphine as part of their initial treatment also receive more laxative and anti-emetic prescriptions compared to patients who do not. These findings underline the inadequacy of management.