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A nationwide study of the extent and factors associated with fentanyl use in Australia

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ABSTRACT

Objective: To examine fentanyl utilisation in the Australian community and determine the geographic and socio-demographic factors associated with higher rates of fentanyl utilisation.
Methods: National sales data (supplied by IMS Health) were used to estimate fentanyl utilisation (in pack sales and milligrams) in Australia during 2013, mapped to Australian Bureau of Statistics (ABS) Statistical Local Areas (SLAs) and Remoteness Areas. Socio-demographic characteristics and total population estimates of SLAs were obtained from the ABS. SLA-level data on sex, age distribution, income, occupations involving physical labour and number of pharmacies, were included in linear regression analyses to examine their association with fentanyl use.
Results: An estimated 12.3 kg (or 859,518 packs) of fentanyl was sold across Australia in 2013, equating to an average of 0.55 mg/person over the year. Transdermal patches accounted for the majority (99%; 850,923 packs) of fentanyl sales. South Australia had the highest rate of utilisation per person. Rates of fentanyl utilisation were higher among more remote areas in three jurisdictions. Overall, higher utilisation rates were observed in SLAs that were less populated (β 0.12; $p < 0.001$) and those with a higher proportion of older people (β 0.12; $p < 0.001$), low-income households (β 0.12; $p < 0.001$) and people working in jobs requiring physical labour (β 0.08; $p < 0.05$).
Conclusions: Transdermal fentanyl patches account for the majority of fentanyl utilisation in the Australian community. There is marked variation in fentanyl utilisation across geographic areas, with higher use apparent in areas with a higher proportion of older people and indicators of greater socio-economic disadvantage.

1. Introduction

The role of fentanyl is well established as a second-line treatment option in the management of severe and chronic pain conditions that are either cancer or non-cancer related.[1,2] Due to the availability of controlled-release formulations and advanced delivery methods, substantial increases in the use of fentanyl worldwide have been observed since the 1990s.[3] Transdermal fentanyl patches in particular, offer an alternative treatment option when oral formulations cannot be tolerated and have the convenience of twice weekly dosing. Consequently, in 2013, fentanyl recorded the highest rate of global consumption in terms of daily doses across all synthetic opioids with an estimated 2.8 billion statistical Defined Daily Doses (or S-DDDs) consumed over the year.[3] Countries currently leading the global consumption of fentanyl are the United States, Germany, Spain, France and Canada.[3] In Australia, fentanyl accounts for 2% of all opioid pack sales in the community and 24% of total use when accounting for potency differences across a common metric (oral morphine equivalents).[4]

The high potency of fentanyl relative to morphine and other pharmaceutical opioids also increases its attractiveness in illicit drug markets. Accordingly, alongside increases in the use of fentanyl, reports of misuse and associated harms have been growing in countries such as the United States, Canada, Australia, Estonia and other parts of Europe.[5–8] Although mortality related to fentanyl is

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currently low in Australia, there is evidence that rates are increasing.[5,9] Many of these deaths appear to be the result of injecting fentanyl extracted from transdermal patches.[9]

In order to minimise potential misuse of transdermal fentanyl patches in the Australian community, one response has been to alert health practitioners in some jurisdictions to be cautious when prescribing and dispensing fentanyl.[10,11] In light of the high potency and rising rates of misuse and overdose related to fentanyl,[5] as well as previous findings highlighting that there is regional variation in strong opioid use across Australia and that use is higher among more disadvantaged communities,[4,12] there is a need to examine the extent of use of fentanyl more broadly across Australia and the factors driving this use. Therefore, the overall aim of this study was to examine fentanyl utilisation in the Australian community, with the specific aims of:

(1) Estimating total fentanyl utilisation across Australia and across different geographical areas and;
(2) Examining the geographic and socio-demographic factors associated with higher rates of fentanyl utilisation.

2. Methods

2.1. Fentanyl sales data

A third party access request to obtain pharmaceutical opioid sales data in Australia was approved by IMS Health. IMS Health collect data on sales of prescription and non-prescription items through pharmaceutical wholesalers and manufacturers who sell direct to pharmacies, representing over 94% coverage of the Australian market.[13] This study focused on fentanyl items sold in the community, representing approximately 5450 pharmacies in operation across Australia between 2013 and 2014,[14] and excluded fentanyl items supplied in hospitals. All fentanyl preparations available in Australia for the indication of pain were included, corresponding to the World Health Organization's (WHO) Anatomical Therapeutic Classification code N02AB03.[15] This included extended-release transdermal patches and immediate-release lozenge formulations.

2.2. Geographic coding

IMS Health data were provided in sales “bricks”, which are geographic boundaries containing clusters of pharmacies, developed for medicine sales and distribution purposes across Australia. Sales bricks were mapped to postcodes, which were then mapped to 2011 Statistical Local Areas (SLAs) using the Australian Bureau of Statistics' (ABS) Australian Standard Geographical Classification system; a total of 1375 SLAs were mapped with total populations ranging between 9 and 148,423 people.[16] SLAs are a method of statistical geographic classification used in the reporting of data from the Australian Population Census.[17] They provide a spatial unit encompassing local government councils and in some cases, unincorporated areas. When combined together, the spatial units are designed to completely cover all of Australia without any gaps or overlaps. SLAs were also coded according to remoteness using the ABS′ Remoteness Areas classification system which takes into account the distance required to travel in order to access different types of service centres.[18,19] These areas are defined as “Major Cities”, “Inner Regional”, “Outer Regional”, “Remote” and “Very Remote”. Where SLAs covered multiple remoteness areas, remoteness was defined on the basis of the category which represented the majority of the SLA. Details of the classification of SLAs according to these groupings can be found elsewhere.[18,19]

2.3. Data on characteristics of Statistical Local Areas

Data on the characteristics of SLAs were obtained from a range of sources. The number of people in each SLA (measured in 10,000s) was calculated from ABS 2012 population estimates.[20] Socio-demographic characteristics of residents in each SLA were obtained from the ABS Census Table Builder Pro.[21] These included: proportion who were male; proportion over 65 years of age; proportion working in jobs involving physical labour (defined as agriculture, mining, manufacturing and construction industries) and proportion of low-income earning households (defined as earning less than AUD$400 per week), which were guided by findings on characteristics common among people with chronic pain conditions in Australia and internationally.[22,23] The number of community pharmacies in each SLA (defined as the number of pharmacies per 1000 persons) was estimated using a marketing database containing details of all pharmacies across Australia.[24]

2.4. Analyses

Analyses were conducted using SAS Enterprise Guide 6.1 (SAS Institute Inc., Cary, NC, USA), STATA 13 (StataCorp LP, Texas, USA), and Microsoft Excel 2010 (Microsoft, Seattle, WA). Fentanyl utilisation was estimated in two ways by totalling: (1) the number of packs sold and (2) the number of milligrams (mg) sold. In order to better represent utilisation of transdermal fentanyl patches in practice, the amount in mg represents the total amount released over three days if used in accordance with prescribing guidelines and manufacturer directions,[25] rather than the total mg contained in the patch. This adjustment is important as depending on specific brands, the estimated amount of active fentanyl released from a patch is approximately 43% of the total amount of fentanyl contained in a patch and would therefore over-estimate actual use.

Once sales data were coded to SLAs and remoteness areas, total fentanyl utilisation was calculated and rates of use per person (mg per person) estimated, based on population data from the ABS.[20] Confidence intervals (95% CIs) were calculated for the estimated number of packs and mg sold per person, by jurisdiction and level of remoteness. A map presenting geographic distribution of fentanyl utilisation (mg per person) by SLA across Australia was generated using the ArcMap component of ESRI ArcGIS software (see Fig. 1).[26]

Bivariate and multivariate linear regressions were undertaken to examine socio-demographic factors associated with the rate of fentanyl utilisation (mg per person) at the SLA level. Variables included in the regression analyses were the number of pharmacies per 1000 persons in SLAs, the number of people in each SLA measured in 10,000s, and the ABS variables representing the characteristics of SLAs listed above (proportion who were male; proportion over 65 years of age; proportion working in jobs involving physical labour and proportion of low-income earning households). Remoteness was not included as a variable in the regression analyses as it was highly correlated with factors such as the number of people in each SLA.

3. Results

3.1. Fentanyl utilisation in pack sales

A total of 859,518 fentanyl packs were sold across Australia in 2013: transdermal patches accounted for 99% (850,923) of all pack sales and lozenges accounted for 1% (8595) of all pack sales. After taking into account population size, approximately 0.04 fentanyl packs were used per person over the year (Table S1). The highest rate of fentanyl utilisation per person was observed in South

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