Codeine dispensing for privately insured children in the USA: a retrospective database study

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ABSTRACT
In this retrospective study using claims data from the OptumLabs Data Warehouse including 24658769 eligible person-years of coverage in the USA, there was substantial decline in codeine dispensing between 2010 and 2019. However, we also observed a persistence of codeine prescribing despite the FDA contraindication. In 2019, codeine was still being prescribed to children aged 12–17 years at 934 prescriptions per 100,000 person-years of coverage and 106 per 100,000 person-years of coverage in children aged <12 years.

INTRODUCTION
Codeine is a prodrug that is metabolised in the liver to morphine to produce analgesia and antitussive effects. The metabolism is based on the cytochrome P450-2D6 (CYP2D6) genotype, which is highly variable and can result in differing amounts of morphine produced. Even with standard dosing, ultrarapid metabolisers will produce significant morphine which may cause respiratory depression and possible death, particularly in children with a history of obstructive sleep apnoea.1–3 Beginning in 2013, the US Food and Drug Administration (FDA) released increasingly restrictive warnings and ultimately recommended against the use of codeine-containing products in patients under age 18 (table 1).4 In this context, little is known about how paediatric codeine prescribing changed over time in the USA, including periods before and after the main FDA Drug Safety Communications (DSC).

METHODS
We performed a retrospective database study of privately insured children (age<18 years) who received one or more prescriptions for codeine, opioids other than codeine or non-opioid cough and cold medications between 1 January 2010 and 31 December 2019. We used pharmacy claims from the OptumLabs Data Warehouse (OLDW), a database containing over 150 million unique individuals across the USA who are privately insured and/or Medicare beneficiaries. The OLDW includes 20% of the commercially insured population in the USA, with similar distributions of age, sex and race or ethnicity to the US commercial population. This study was deemed exempt from review by the Institutional Review Board.

We analysed prescriptions dispensed in children aged<12 years and those aged 12–17 years (same age groupings used in codeine-related FDA DSCs). Descriptive statistics are reported as prescriptions dispensed per 100,000 age-group person-years of coverage.

Patient and public involvement
There was no patient or public involvement in this study.

RESULTS
We identified 24658769 eligible person-years of coverage. Codeine dispensing declined over the entire study period in both children under 12 years and those aged 12–17 years. In children<12 years, codeine dispensing decreased 97.2% (from 3760 in 2010 to 106 per 100000 person-years of coverage in 2019). In older children aged 12–17 years, codeine dispensing decreased 78.9% (from 4435 in 2010 to 934 in 2019). These declines were greater than the declines in opioids other than codeine (age<12 years, declined 58.3% from 2104 to 877; age 12–17 years, declined 61.4% from 10439 to 4031). They were also greater than the changes in non-opioid cough and cold medications (age<12 years, declined 52.6% from 7980 to 3784;...
age 12–17 years, increased 39.8% from 3149 to 4400). For both age groups, the largest single-year decline in codeine dispensing was from 2017 to 2018: for children<12 years, codeine dispensing declined 61.2% (from 586 to 228); for children aged 12–17 years, codeine dispensing declined 38.1% (from 2094 in 2017 to 1295 in 2018). Figure 1 illustrates these trends. Trends of codeine prescriptions separated by pain or cough indications are available in online supplemental file 2.

**DISCUSSION**

Codeine dispensing in children has declined substantially between 2010 and 2019, including the most severe restriction in early 2018 during which the FDA made codeine contraindicated. These relative declines were specific to codeine versus other opioids and versus non-opioid cough and cold medications and were greatest in the year the most severe restriction was issued. While FDA restrictions were temporally associated with a decrease in codeine use, prescribing was already declining prior to the first DSC for both codeine and non-codeine products. In 2019, codeine was still being prescribed to children aged 12–17 years at 934 prescriptions per 100,000 person-years of coverage and 106 per 100,000 person-years of coverage in children aged<12 years. Other studies have also showed the persistence of codeine prescribing despite an absolute FDA contraindication. Efforts to
cease the use of codeine in paediatric patients need to continue.

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