

Opioids are one of the most important and effective drugs in pain medicine with a key role in modern anaesthesia, palliative care, emergency medicine and specialised pain management. Although prescriptions of opioids are beneficial for managing chronic pain, they often lead to misuse or abuse, increasing the risk of public health consequences. In fact, the increase of opioid prescription over the past decade has led to higher numbers of analgesic opioids misuse, abuse and opioid-related deaths in most developed OECD countries. Considering Germany and France are two of the largest economies and the most populated countries in the European Union, the study of prevalence of analgesic opioids use and patterns in opioids prescription within these countries is crucial in the light of global opioid epidemic. The aim of this work is to provide evidence-based inputs from a systematic review of relevant literature in order to better inform adequate prevention strategies.

Patterns in analgesic opioids use in Germany and France:

improved pain management and risks of misuse



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Methods :

A systematic literature review of the prevalence of analgesic opioid use and patterns in opioid prescription in Germany and France between 2000 and 2017 was conducted, searching PubMed, Web of Science and Wiley Online Library. The review included peer-reviewed and grey literature in English, German and French. Studies were selected upon meeting predefined eligibility criteria (Table 1). Additionally, a web search engine (Google.com) was employed to also include grey literature.

Table 1. Inclusion and exclusion criteria for study selection

Inclusion criteria	Exclusion criteria
1. Full-text accessible at University of Cambridge & Maastricht University	1. Full-text not accessible at University of Cambridge or Maastricht University
2. Language: English, German, French	2. Languages other than English, German or French
3. Geographic area: France & Germany	3. Studies focused on children or adolescents
4. Epidemiological data stating prevalence and/or incidence of outpatient opioid prescription	4. Studies strictly referring to one specific opioid (e.g. tramadol, fentanyl)
5. Studies on general opioid prescription / prescription of certain groups of opioids	5. Studies solely referring to hospital opioid use

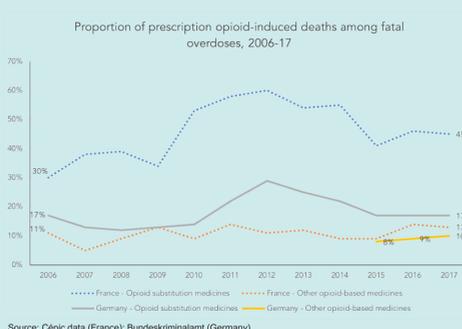
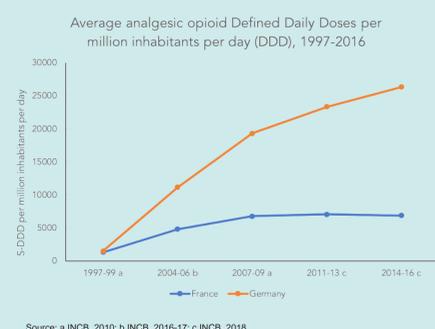
Table 2. Prescription of analgesic opioids in France and Germany, 2000-17: Main indicators

	France	Germany
Prevalence of Prescription Opioids (PO)	19.2% (2004) - 17.5% (2017) (1) 17.1% (2015) (3)	0.54% (2000-03) (2) 5.7% (2004) - 5.9% (2009) (4) 1.3% ** (2012) (5) - 1.6% (2016) (6)
Prevalence of mild PO	19.1% (2004) - 17.1% (2017) (1) 16.7% (2015) (7)	5.08% (2004) - 4.94% (2009) (4) 0.92% (2015) (7)
Prevalence of strong PO	0.54% (2004) - 1.1% (2017) (1) 0.92% (2015) (7)	1.08% (2004) - 1.43% (2009) (4) 1.39% (2011) (8)
DDD 1000 inhabitants-1 day-1 (mild PO)	16.2 (2004) - 15.1 (2017) (1) 28 (2015) (10)	3.67 (2002) (9)
DDD 1000 inhabitants-1 day-1 (strong PO)	1.7 (2004) - 2.7 (2017) (1) 2.8 - 3.2 (2015) (10)	2.086 (2011) (8)
Tramadol	Prevalence 4.1% (2004) - 8.4% (2017) (1) 7.51 (2004) - 11.22 (2017) (3)	29% (2002) (9) 98% (2015) (10)
Codine	Prevalence 3% (2004) - 6.8% (2017) (1) 6.45 (2004) - 7.65 (2017) (3)	
Opium	Prevalence 1.7% (2004) - 5.3% (2017) (1) 2.11 (2004) - 4 (2017) (3)	
Fentanyl	Prevalence 0.19% (2004) - 0.33% (2017) (1) 0.28 (2004) - 0.62 (2017) (3)	40.8% (2011) (8)
Morphine	Prevalence 0.4% (2004) - 0.5% (2017) (1) 1.03 (2004) - 0.97 (2017) (3)	13.5% (2011) (8)
Oxycodone	Prevalence 0.02% (2004) - 0.41% (2017) (1) 0.12 (2004) - 0.85 (2017) (3)	12.8% (2011) (8)

* CNCP patients only
** LTOT for non-cancer patients only

Our electronic search yielded 895 articles. Two levels of screening by two independent researchers were used on all citations, resulting in a final selection of 10 articles and 1 official report. Disagreement was resolved by face-to-face discussion, leading to a consensus judgement. Due to the small number of included studies and the heterogeneity in study methodology, the appropriateness of a meta-analysis may have been critically questioned and therefore, was not included as part of this study.

The quality of studies was assessed using the EPHPP (Effective Public Health Practice Project) quality assessment tool for quantitative studies. Overall, the evidence base was rated as moderate. However, the applied tool might not be ideal for rating the quality of studies on secondary data such as insurance claims data and medical records since some of the assessed components seem to be inappropriate (e.g. data collection methods or blinding).



Results :

For Germany and France, the analysed data were mainly extracted from national insurance claims databases and national authorities' registers. In the framework of a tightly regulated use, the reviewed literature suggested an increase in the prescription of strong opioids (+29% in Germany between 2006-11; +104% in France between 2004-17), to the detriment of mild prescription opioids (-2.8% in Germany and -10.5% in France during the same periods).

In parallel, the average availability of analgesic opioid Defined Daily Doses per million inhabitants per day (DDD) has steadily increased in both countries from less than 2 000 DDD in the late 1990s to more than 26 000 in Germany (+1657%) and around 6 800 in France (+416%) in 2014-16. In terms of consumption, of number DDD per 1000 inhabitants has decreased for mild PO from 59,1 to 24,3 in France (-143%) while it increased from 2 to 2,9 for strong PO (+45%). In Germany, DDDs 1000 inhabitants-1 day-1 was 3,67 for mild PO in 2002 and 2 086 for strong

The majority of opioid prescriptions seemed to be for patients with chronic non-cancer pain (CNCP) in both countries (around 80% in Germany and 68%-78% in France).

In both Germany and France, analgesic opioids were primarily prescribed by general practitioners (86% in 2011 and 87% in 2017 respectively) and orthopaedists (3,8% and 1,8% respectively). Interns accounted for 4% of dispensed analgesic opioids in Germany, and dentists for 2,4% in France.

In France, opioid use tended to be more common among people aged 65 years-old or more (27% of PO users in 2017) and women (57%). In Germany, 71% of new users of fentanyl patches were women in 2011. No further details were given to underpin sociodemographic comparisons.

In both countries, **tramadol (alone or in combination) was the most commonly used mild opioid** (98% of mild opioid prescribed in Germany in 2015, 49% in France in 2017). According to data available for France, the prevalence of tramadol use doubled between 2004-17 (from 4,1% to 8,4% of the French population), while the number of DDDs 1000 inhabitants-1 day-1 increased by 49% between 2006-17 (from 7,51 to 11,22). **Fentanyl as emerged as the most prescribed strong opioid in both countries** (40% of strong opioid prescribed in Germany in 2011-15, 32% in France in 2017). In France, prevalence of fentanyl use (transmucosal and transdermal forms) increased by 74% between 2004-17 (from 0,19% to 0,33% of the French population), and the number of DDDs 1000 inhabitants-1 day-1 more than doubled between 2006-17 (0,28 to 0,62). Finally, the prescription of oxycodone represented 13% of strong PO in Germany in 2011 and 39% in France in 2017. In this country, the use of **oxycodone showed the most remarkable increase since 2004**, both in terms of prevalence of use (from 0,02% to 0,41%, +1950%) and regarding the number of DDDs 1000 inhabitants-1 day-1 (from 0,12 to 0,85, +608%).

Although the prescription of analgesic opioids has increased in Germany over the last decade, with the country being the second user of prescription opioids in Europe in 2017, the share of opioid-related deaths (namely opioid substitution medicines) has remained stable at around 17% over the last decade. Since 2015, Germany has been registering fatal overdoses as a result of the use of opioid-based medicines (including fentanyl) and synthetic opioids (since 2016). Opioid-based medicines represented 8% of fatal overdoses in 2015, reaching 10% in 2017.

In France, while the overall use of analgesic opioids has decreased, the misuse of prescription opioids (namely opioid substitution medicines) and the number of opioid-related deaths have been on the rise. Between 2000-17, the number of PO-related hospital admissions per million population grew from 15 to 40 (+160%), and the share of PO-induced deaths among poisoning deaths increased from 41% to 58% from 2006-17 (+41%).

Over the last decades, the overall prevalence of analgesic opioids use has increased in Germany while it has decreased in France. In the case of France, the downward trend may partly be explained by the suspension of marketing authorization for dextropropoxyphene and its subsequent.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the work.

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