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Review Article

The Opioid Epidemic in Numbers: A Meta-Analytic Review of Mortality, findings, and Implications for Prevention

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Abstract

The opioid crisis in North America, particularly the United States and Canada, has been characterized by increasing methadone distribution, overdose deaths and diversion, although recent efforts have seen declines in some areas. Canada's prescription opioid dispensing increased until 2012, after which areas such as Ontario saw significant declines. The United States experienced a staggering 345% increase in opioid-related deaths from 2001-2016, heavily affecting people aged 25-34. This growing epidemic is further highlighted by the U.S. National Survey, which shows that 8.9% of Americans aged 12 or older engaged in illicit drug use recently. Research links opioid sales to overdose deaths, highlighting the dangers of inappropriate prescription practices. To address this, Medication-Assisted Treatment (MAT), behavioral therapies and support groups are promoted. Anti-stigma interventions such as acceptance and commitment therapy and motivational interviewing have been shown to be effective. A consistent pattern observed in cities such as Philadelphia and San Francisco indicate that young heroin addicts often switch from pharmaceutical opioids to heroin, driven by the economics of drug supply. To address opioid use disorders, primary care has recognized MAT as critical, with new innovative models such as multi-level care and stakeholder engagement. Nevertheless, barriers such as stigma and lack of expertise pose challenges, highlighting the urgent need for refined strategies and models tailored to different primary care settings.

Keywords: MAT; Opioids; OUD; Prevention devices; Stigma

Background

Originally used for opioid use disorders, methadone has gained traction in pain management, raising concerns about the risks of overdose and potential abuse. The opioid crisis has intensified globally, with countries like Canada and the United States witnessing skyrocketing opioid prescriptions and related harm. In Canada, where prescription opioid use is second only to the United States, new studies have documented extensive opioid-related harms, from nonmedical use to increased morbidity and mortality. The US opioid epidemic deepened between 2010-2015, with overdose deaths especially from synthetic opioids such as illegally manufactured fentanyl. The resulting health burden is alarming; Opioid addiction led to nearly 1 million disability-adjusted life years lost annually in North America in 2010. Considering the degree of severity, studies have sought optimal treatment strategies. Opioid substitution treatments, such as methadone and buprenorphine, are showing promise in reducing opioid harm. But methadone's overdose risk and buprenorphine's subpar retention rate pose challenges. Another obstacle is the stigma surrounding substance abuse disorders, which hinders access to healthcare and affects the quality of care. The history of the opioid crisis can be traced back to the 1990s when the introduction of Colombian heroin into the eastern United States resulted in increased purity and reduced prices. Purdue Pharma's aggressive marketing of OxyContin in 1995 and its subsequent increase in sales played a significant role. The transition from prescription opioids to heroin, particularly among younger individuals, further exacerbated the crisis. Understanding these trajectories and identifying effective

interventions is critical for global public health.

Methods

Retrospective Observational Study, 2002-2014 [1], USA: Retrospective analysis of methadone distribution, diversion and overdose deaths over 12 years. National databases such as the National Vital Statistics System, Prescription Drug Monitoring Programs, and any law enforcement reports. Variables: Addiction: Methadone-related overdose deaths, methadone diversion. Independent: Year, methadone prescription rates, demographics, confounding factors. Fischer et al. (2014, Canada) [2]: Design: Retrospective analysis of prescription opioid dispensing. Data sources: Representative sample of pharmacies across Canada. Period: 2005-2012. Guy et al. (2016, United States) [3]: Design: Retrospective analysis of opioid prescribing data. Data sources: National sample of retail pharmacies, IMS Lifelink+ database. Sample: 10% sample of patient records 2006-2015 [4]. Inclusion/exclusion: Included patients ≥18 years of age with at least one opioid prescription. Excluded cancer patients, addiction disorder or those prescribed buprenorphine for addiction treatment. Analysis: Kaplan-Meier statistics, sensitivity analyses.

Literature review (Canada): Design: Review focusing on PO-related studies/data after 2010 [5] or relevant earlier data. Data sources: Key databases, gray literature (eg government reports). Sections: PO Dispensing/Use, Nonmedical PO Use, PO-Related Morbidity/Mortality, and Interventions/Effects.

Cohort study on opioid dependence: Design: Cohort study on opioid dependence regarding methadone or buprenorphine treatment. Data sources: Databases such as Medline, Embase etc. and expert consultations. Inclusion/Exclusion: Included cohort studies on opioid-dependent individuals. Excluded non-original research, non-cohort studies, non-human studies, among others. Analysis: Mortality rates, meta-regression models, sensitivity analyses. Opioid-related Death Assessment (2001-2016, USA): Design: Analysis of opioid-related deaths. Data source: CDC WONDER database. Analysis: Opioid mortality in specific years using the Cochran-Armitage test for trend. MAT Models of Care Review: Design: Systematic review of MAT models Data sources: Electronic databases from 1995 to mid-June 2016, gray literature, and key informant interviews. Stigma and substance abuse study: Design: Review of interventions against stigma and substance use disorders. Data sources: Seven electronic databases, manual searches, expert consultations. Review process: Double-blind review, assessment of inter-rater agreement. Analysis: Descriptive synthesis due to heterogeneity. Heroin Price and Purity Study (HPPO): Design: Ethnography and interviews on heroin use, focusing on Philadelphia and San Francisco. Method: Targeted selection, interviews in user environments and NVivo software for data organization [6-13].

Results

Methadone trends, 2002-2014: Increase in methadone distribution for pain, indicating its acceptance compared to other opioids. At the same time, reports of methadone diversion increased, pointing to abuse or a black market. A potential increase in methadone-related overdose deaths during the study period, potentially linked to increased prescribing and diversion. Demographic insights show that certain age, gender or region may be more affected by methadone overdose.

Canadian Opioid Trends (2005–2013): Dispensing of prescription opioids increased by 2.6% annually until 2011, and slowed in 2012. A decrease in strong opioids was noted in four provinces. Significant differences between provinces were observed, with Ontario showing the highest prescribing rate and Newfoundland and Labrador the lowest.

US Opioid Trends (1999–2015): Opioid prescribing peaked in 2010 and remained higher than in 1999, with long-acting opioids such as oxycodone seeing the biggest decline. There was wide geographic variation in prescribing rates, higher in rural areas and in states with more Medicaid workers. Notably, the prescription rate was 81.2 per 100 in 2010, and fell to 78.5 in 2015. Insights into mortality and treatment: Opioid substitution treatments, such as methadone and buprenorphine, significantly reduced mortality. However, mortality increased upon cessation. From 2001 to 2016, opioid-related deaths in the US increased by 345%.

Demographic and Drug Use Patterns (2010 and 2015): In 2010, 22.6 million Americans were illicit drug users. In 2015, drug overdoses accounted for 52,404 deaths in the United States, of which 63.1% involved an opioid.

Medication-Assisted Treatment (MAT) and stigma studies: Twelve MAT models in primary care were identified, emphasizing pharmacological treatment, psychosocial interventions and educational outreach. Thirteen studies evaluated stigma, most using education and/or direct contact with addicts. Interventions generally produced positive results against stigma.

Ethnographic Insights (Philadelphia & San Francisco): Philadelphia saw a surge in young heroin addicts switching from opioid pills. Most users in Philadelphia were local and involved in drug markets. In contrast, San Francisco had a varied user base with many migrants, with many involved in selling marijuana. In summary, the opioid epidemic has various facets, from prescription trends to treatment effectiveness, demographics, and societal consequences. Addressing the problem properly requires multifaceted strategies tailored to regional and demographic needs.

Conclusion

The US has seen a decline in methadone distribution, overdose

deaths, and diversion after 2006 due to increased risk awareness, regulatory changes, and modifications to clinical guidelines. Despite the decline, older individuals, especially those aged ≥55 years, remain at risk. The increase in methadone distribution for pain brings therapeutic gains and challenges, with associated overdose deaths emphasizing the necessity of strict monitoring and patient education. Studies note that while opioid prescribing trends in Canada and the United States show positive changes, discrepancies in interprovincial and geographic prescribing patterns remain. Rapid transition from acute to chronic opioid use, often after limited initial use, emphasizes prudent prescribing and patient education about long-term risks. Opioid-related mortality, especially among young adults, men and the 55-64 age group, requires urgent interventions. In treatments, opioid substitution with methadone or buprenorphine shows a significant reduction in mortality. However, the first month after starting or stopping these treatments shows an increased risk of mortality. The opioid crisis in the US is pronounced, with prescription opioids now leading to more deaths than any major cause combined. Predominantly, deaths occur due to prescribing within guidelines, revealing inappropriate prescribing patterns, often due to misinformation and misperceived safety. Interventions targeting substance use disorder stigma show promise but require more research for sustained efficacy. The ease of obtaining opioid pills has indirectly escalated heroin use, as individuals switch to heroin when their preferred pills become unavailable. This direct development requires comprehensive public health measures, taking into account both evolving supply factors and the demographics of the risk zone.

Prevention

To mitigate the harms associated with prescription opioid use, educating healthcare providers about the risks, benefits, and best practices of opioid prescribing is imperative. Developing robust guidelines for safe and judicious use, along with improved access to evidence-based treatments for Opioid Use Disorders (OUD), is critical. Raising public and professional awareness of the dangers of opioid overdose and the lifesaving potential of naloxone can further protect communities. For acute pain management, opioid therapy should be limited, preferably not exceeding one week, and healthcare professionals should engage in thorough patient discussions about the implications of long-term use. Promotion of Medication-Assisted Treatment (MAT) – recognized as the most effective treatment for OUD – must be at the forefront of intervention strategies, emphasizing its role in reducing opioid use and overdose deaths. Comprehensive responses should also include distribution of naloxone, expansion of non-opioid pain management techniques, use of prescription drug monitoring programs, and promotion of a collaborative approach between public health and safety units. In addition, early detection, screening, and proactive interventions in healthcare settings, as well as community engagement, are essential to prevent OUD escalation and emphasize MAT benefits.

To address the risks of prescription opioid use, education for healthcare providers about prescribing risks, benefits, and best practices is essential. Enacting comprehensive guidelines for safe opioid use and expanding access to evidence-based OUD treatments is critical. Awareness of the dangers of opioid overdose and the effectiveness of naloxone is paramount. Acute pain management should limit opioid use, with informed discussions of implications for long-term use. Prioritizing medication-assisted treatment (MAT) as the primary OUD treatment is necessary due to its proven effectiveness in curbing opioid abuse and overdose deaths. Effective prevention measures include distribution of naloxone, promotion of non-opioid pain relievers, use of prescription monitoring programs, and promotion of public health and safety cooperation. Early OUD detection and community involvement improve the prevention effect. Tools such as Narcan nasal spray, opioid overdose prevention devices, smartphone apps, Masimo Opioid Halo, and capnometers offer important support in monitoring and combating opioid overdoses.

Limitation

The analyzed studies showed several limitations. Predominantly, many focused solely on prescription data for opioids and neglected opioids obtained outside of healthcare, such as nonmedical prescriptions or illicit use. In addition, the reasons behind the observed trends were not always investigated, including the impact of recent public health interventions. Key information, such as actual dose titration, intent behind chronic opioid use, pain intensity, duration and cause, was often not considered. Some research lacked systematic review standards or meta-analytic techniques due to data heterogeneity. Methodological shortcomings, such as potential confounding during treatment transitions and misclassifications such as falsely attributing deaths, were evident in some studies. Many studies were limited to high-income countries, suggesting a data gap for low- and middle-income countries. The accuracy of opioid-related death records was another concern, with variations between states and potential underreporting or misclassification. The limitation of some analyzes to limited jurisdictions limited generalizability. Studies often emphasized drug comparisons over MAT model efficacy, and real-world implementation barriers remained insufficiently addressed. Finally, some reviews faced challenges due to different study methods, language limitations, and inherent biases in qualitative research, despite efforts to mitigate these biases.

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