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We recently published a study of postsurgical prescriptions for opioid and their association with overdose and misuse, We're Gabriel Brat and Denis Agniel, AMA!

OPIOID_ABUSE [R/SCIENCE](#)

The United States is currently experiencing an opioid crisis. The [CDC website](#) has some chilling facts: The majority of drug overdose deaths (66%) involve an opioid. In 2016, the number of overdose deaths involving opioids was 5 times higher than in 1999. From 2000 to 2016, more than 600,000 people died from drug overdoses. On average, 115 Americans die every day from an opioid overdose. Despite all this, opioids remain an effective treatment for post-operative pain. Surgeons struggle with adequately treating their patients' pain needs while being mindful of the risks of opioids. Not enough is known about the risks of treating patients with longer durations and stronger doses of opioids.

In our [paper](#) published in the BMJ, we quantified the association between the amount of opioids patients received directly after surgery and the rate of misusing opioids (including overdose, abuse, and dependence) in more than 500,000 surgery patients enrolled in commercial medical insurance who received opioids. We found that each additional refill a patient received was associated with a more than 40% increase in the rate of misuse and each additional week of opioids with a 20% increase. The dose of opioids had a much smaller impact and only seemed to become important among patients who used opioids for an extended period.

Those numbers are based on statistical models that take into many factors about the patients, including their surgery type, age, sex, and certain diagnoses that they might have received before surgery like tobacco use disorder or depression. To give you a sense of some related unadjusted data, 0.18% of patients with no refills experienced a misuse event within one year after surgery. That number doubles to 0.37% among those who filled just one additional opioid prescription after surgery. And it jumps all the way to 1.1% among those with more than 5 refills. Our main analysis included all misuse events (not just those that happened within one year after surgery) and showed very similar results.

AMA!

We are:

Gabriel Brat, instructor in surgery and in biomedical informatics at Harvard Medical School and a trauma surgeon at Beth Israel Deaconess Medical Center

Denis Agniel, associate statistician at the RAND Corporation and part-time lecturer at Harvard Medical School

Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study BMJ 2018; 360 doi: <https://doi.org/10.1136/bmj.j5790>

Edit: Thanks everyone for all the questions. We are signing off now, but we will check in later to participate in further discussion.

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CORRESPONDENCE:

DATE RECEIVED:

February 15, 2018

You claim a huge number of overdose deaths. Those deaths are not thoroughly researched. Leading addiction expert Dr. Carl Hart says the majority of opioid deaths are due to a lack of knowledge resulting in adverse reactions (like opioid + alcohol). I think your stats are misleading as they cannot truly be nailed down as overdose deaths.

Also you give the percent change up front in your abstract and the summary here for WOW factor. We

DOI:
10.15200/winn.151861.12687

ARCHIVED:
February 14, 2018

CITATION:
Opioid_Abuse , r/Science , We recently published a study of postsurgical prescriptions for opioid and their association with overdose and misuse, We're Gabriel Brat and Denis Agniel, AMA!, *The Winnower* 5:e151861.12687 , 2018 , DOI: [10.15200/winn.151861.12687](https://doi.org/10.15200/winn.151861.12687)

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see the addiction rate is about 0.6% from your data. THE ADDICTION RATE IS SUPER LOW. Why are you trying to be misleading by focusing on trivial changes between 0.1 and 1.1%? You should be talking about how addiction isn't due to the drug itself but more to socioeconomic status and anxiety to help other addiction experts rid our society of backwards views.

Legalize and educate.

Thanks for the paper that reveals the rate of opioid abuse stemming from prescribed opiates is under 1%!

[Uruk-high](#)

Thanks for the paper that reveals the rate of opioid abuse stemming from prescribed opiates is under 1%!

To be clear, our study looks at opioid-naive patients who undergo surgery and then receive post-discharge opioids. Our outcome metric is dependence, abuse, and overdose. It is not a general analysis of rates of abuse in the broader population. We don't hide the low rate of misuse in this specific population. In fact, it is well documented in several other studies. We specifically address the fact that risk rises rapidly with increased use. That is the critical point. The importance of the work is not to demonize patients who use opioids, but to focus on the correlations--a stronger focus on duration of treatment over dosage in the immediate post-discharge period--that are associated with long-term risk. Both patient, clinical, and broader risk factors definitely have a role in determining the likelihood of misuse. Our paper identifies several external features in the comprehensive model, but the focus of the paper is to better understand the levers of duration and dosage in opioid prescribing. Our goal was and is to provide surgeons and patients with tools to understand how to better reduce risk while addressing pain.

Does this study take into account individuals that abuse opioids, based on the definition that abuse is anything outside prescribed instructions, but develop no dependency? Like individuals who save pills after pain is gone so they can "have fun" at some future time, but don't ever seek more from either docs or the street.

I've always wondered where recreational drug users that do not form dependencies with their drug(s) of choice fall out in the grand scheme of medical stats.

[ecogeek1229](#)

We used a large health insurance claims database to extract defined diagnoses of opioid overdose, abuse, and dependence. A clinician needed to identify a patient as having one of these diagnoses for us to see this information in the database. Recreational drug users may not be identified if this was not recognized by a clinician.

There's been talk of replacing all (or as many as possible) opioids with non-steroidal anti inflammatory drugs (NSAIDs) to treat pain. Are they as effective? Are there any other alternatives that seem promising?

[TuckRaker](#)

The push has been for multi-modal therapeutic regimens, which include NSAIDs as well as things like rest, ice, and breathing practices. There's been a clear appreciation that the majority of patients need a lot less opioids than are being prescribed. There are a subset of surgeries, orthopedic surgery possibly being one, where opioids have a very important role. But there's no question that the majority of

opioids can be replaced with adjuvants. Recent literature has suggested that, under current opioid prescribing practices, the vast majority of opioids (around 80%) go unused.

What do you think would be a more effective approach for post-surgical opioid use concern - reduction in prescription or better identification of potential abuse (case by case)?

[adenovato](#)

Certainly both approaches could be effective and are probably necessary. There may be some cases where identification may be difficult or not possible based on the information available to the surgeon. Further, our study suggests that misuse rates increase dramatically as exposure to opioids increases, so reducing prescriptions may be an easier and more broadly applicable option for influencing misuse in this population.

Can you comment on the direction of the association? Do you think that the duration or number of pills is increasing the risk of later abuse or do you think people who already are abusing drugs are more successful in getting additional or larger prescriptions?

[SalutaryElixir](#)

This is an important point. Because we didn't (and couldn't ethically) run a randomized trial, it is unfortunately difficult to make strong causal claims about the direction of the association. That being said, we did extensive sensitivity analyses to try to establish the validity of our findings. In particular, one of our sensitivity analyses attempted to mimic the results we might see if we were able to take into account an important patient characteristic that we were not able to measure (like a predisposition to misuse) that was both strongly associated with the duration of opioids received and strongly associated with misuse. Even when we included this covariate in our model, we still saw a strong association between misuse and the duration of exposure. This is suggestive that the direction of causation may be from duration to misuse. That being said, much more research is left to be done on this topic.

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k_thx, The questions you posed were the fuel for our study. As a surgeon, I felt the dilemma that exists when trying to work with patients who request refills. On one hand, I know that persistent opioid use is associated with an increased risk of misuse, but I also want to bring comfort to my patients. Our study quantifies the risk associated with that refill so that we can have a more open conversation about the risks of further opioid use. There needs to be a decision made with by both patient and practitioner. Additionally, to me, our work suggests that we should consider earlier referrals to pain specialists--in particular when patients have significant pain well outside the expected window and a complication has been ruled out. This also highlights that we shouldn't be prescribing to the outlier users for the majority of our patient--a difficult situation that it sounds like you encountered despite your best efforts. There is no easy answer to this complicated problem. A personalized and open conversation that balances risks is necessary if we're going to reduce rates of overprescribing and the risks associated with post-surgical use. Finally, as mentioned, setting appropriate expectations is central to this conversation.