BMJ 2017;356:j1224 doi: 10.1136/bmj.j1224 (Published 2017 March 14)

EDITORIALS

The growing problem of co-treatment with opioids and benzodiazepines

A powerful example of potentially dangerous low value care

Pinar Karaca-Mandic *associate professor*[1], Ellen Meara *professor*[2], Nancy E Morden *associate professor*[2]

[1]Division of Health Policy and Management, University of Minnesota School of Public Health, Minneapolis, MN 55455-0381, USA; [2]Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, Hanover, NH 03755-1404, USA

Since 1999, the US has witnessed a fourfold increase in deaths from overdose involving prescription opioids,[1] a fact widely known by US residents. That benzodiazepines are present in over 30% of overdoses involving prescription opioids is less well known.[2]

Using claims based data from 315 428 privately insured individuals in the US with at least one filled prescription for an opioid in 2001-13, Sun and colleagues (doi:10.1136/bmj.j760) examined the prevalence of a hazardous prescription combination.[3] The risk of combining opioids and benzodiazepines has long been understood; both drug classes can be sedating, suppress respiratory efforts, impair thought, slow response time, and increase falls.[2] Sun and colleagues found an alarming rise in this prescribing practice in their study population, from 9% in 2001 to 17% in 2013. They report a significantly increased risk of overdose among patients receiving both drug types concurrently, documenting one type of harm associated with this unsound and growing clinical practice.

The study emerges at a time when clinicians are increasingly engaging in dialogue about low value care—care that is not evidence based and is potentially harmful, unnecessary, or redundant.[4] Attention to low value care expands existing efforts to systematically measure and improve quality of healthcare. Early quality metrics focused on errors of omission, such as missed opportunities to screen for cancer or to vaccinate; more recent initiatives target overuse of health services or errors of commission. This shift has been advanced in the US by the Choosing Wisely campaign.[5]In October 2016, Britain's Academy of Medical Royal Colleges launched a similar program, Choosing Wisely UK.[6] Other countries are likewise working to explicitly define low value care as a first step to reducing it.

Most definitions of overuse of healthcare focus on a single service in a specific population of patients. Common definitions of overuse related to prescription drugs identify one drug class in a narrowly defined group of patients (such as benzodiazepines prescribed to older adults for insomnia or agitation).[7] Choosing Wisely lists, to date, do not include drug-drug combinations such as benzodiazepines and opioids. Hazardous treatment combinations probably represent an important and relatively common form of low value care. Such practices could serve as powerful and measureable indicators of poor quality. Hazardous drug-drug combinations could be among the most readily identifiable forms of risky treatment combinations.

Concern about concurrent use of opioids and benzodiazepines led two US government agencies to act in 2016. The Centers for Disease Control and Prevention (CDC) guidelines on opioid prescribing urge clinicians to avoid concurrent prescribing of benzodiazepines and opioids,[2] and the Food and Drug Administration (FDA) now requires black box warnings (the highest level of alert) on product labels and patient focused medication guides for opioids and benzodiazepines, recognizing the adverse outcomes associated with their concurrent use.[8]

Warnings and guidelines, while important to defining problematic practice, are not likely to change clinical behavior, at least not quickly. Performance metrics used by payers could prove a key lever for change. In the US and the UK, payers hold clinicians and facilities accountable for basic quality. But we found no example of performance metrics targeting hazardous drug combinations. Optimal use of safety alerts in electronic health records could prove effective, but only if they appropriately notify prescribers of hazardous combinations and only if prescribers are held accountable for over-riding warnings. Guidelines provide explicit definitions of best practice, but, as with all else in healthcare, the challenge is in effective implementation and incentives sufficient to motivate changes in the system.

Although implementation of expanded quality metrics, incentives, and systems that facilitate safer prescribing practice

Correspondence to: P Karaca-Mandic pkmandic@umn.edu

around drug combinations will take time, Sun and colleagues provide evidence that can be of immediate use.[3] For example, the risk of overdose was 71% higher in chronic users who concurrently used a benzodiazepine compared with chronic users who did not (5.36% *v* 3.13%). Clinicians caring for patients using opioids chronically need to be especially cautious. Research shows that opioids are prescribed by multiple providers,[9] a situation more common in deaths from overdose when both opioids and benzodiazepines were being taken.[2] Providers can incorporate such evidence into practice rapidly with the right systems in place.

Unless systems are set up to push information to providers, however, busy clinicians will struggle to keep up with their patients' use of different prescriptions. For example, current state monitoring programs for prescription drugs in the US require separate computers with separate authentication, one of many reported barriers to use.

A multi-pronged effort from both regulators and experts writing clinical guidelines, along with extensive expansion in warnings about the hazards of drug-drug interactions, are essential to reduce low value, potentially dangerous care.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: none.

Provenance and peer review: Commissioned; not peer reviewed.

1 Centers for Disease Control and Prevention. Injury Prevention and Control: Opioid Overdose. https://www.cdc.gov/drugoverdose/data/index.html.
2 Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. *JAMA* 2016;356:1624-45. doi:10.1001/jama.2016.1464. pmid: 26977696.
3 Sun EC, Dixit A, Humphreys K, Darnall BD, Baker LC, Mackey S. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. *BMJ* 2017;356:j760.
4 Colla CH. Swimming against the current--what might work to reduce low-value care?*N Engl J Med* 2014;356:1280-3. doi:10.1056/NEJMp1404503. pmid:25271601.
5 An Initiative of the ABIM Foundation. http://abimfoundation.org/what-we-do/choosing-wisely
6 Choosing Wisely UK. http://www.choosingwisely.co.uk/.
7 American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2012;356:616-31. doi:10.1111/j.1532-5415.2012.03923.x. pmid: 22376048.
8 FDA Requires Strong Warnings for Opioid Analgesics, Prescription Opioid Cough Products, and Benzodiazepine Labeling Related to Serious Risks and Death from Combined Use. 2016. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518697.htm.
9 Jena AB, Goldman D, Weaver L, Karaca-Mandic P. Opioid prescribing by multiple providers in Medicare: retrospective observational study of insurance claims. *BMJ* 2014;356:g1393. http://www.ncbi.nlm.nih.gov/pubmed/24553363. doi:10.1136/bmj.g1393 pmid:24553363.