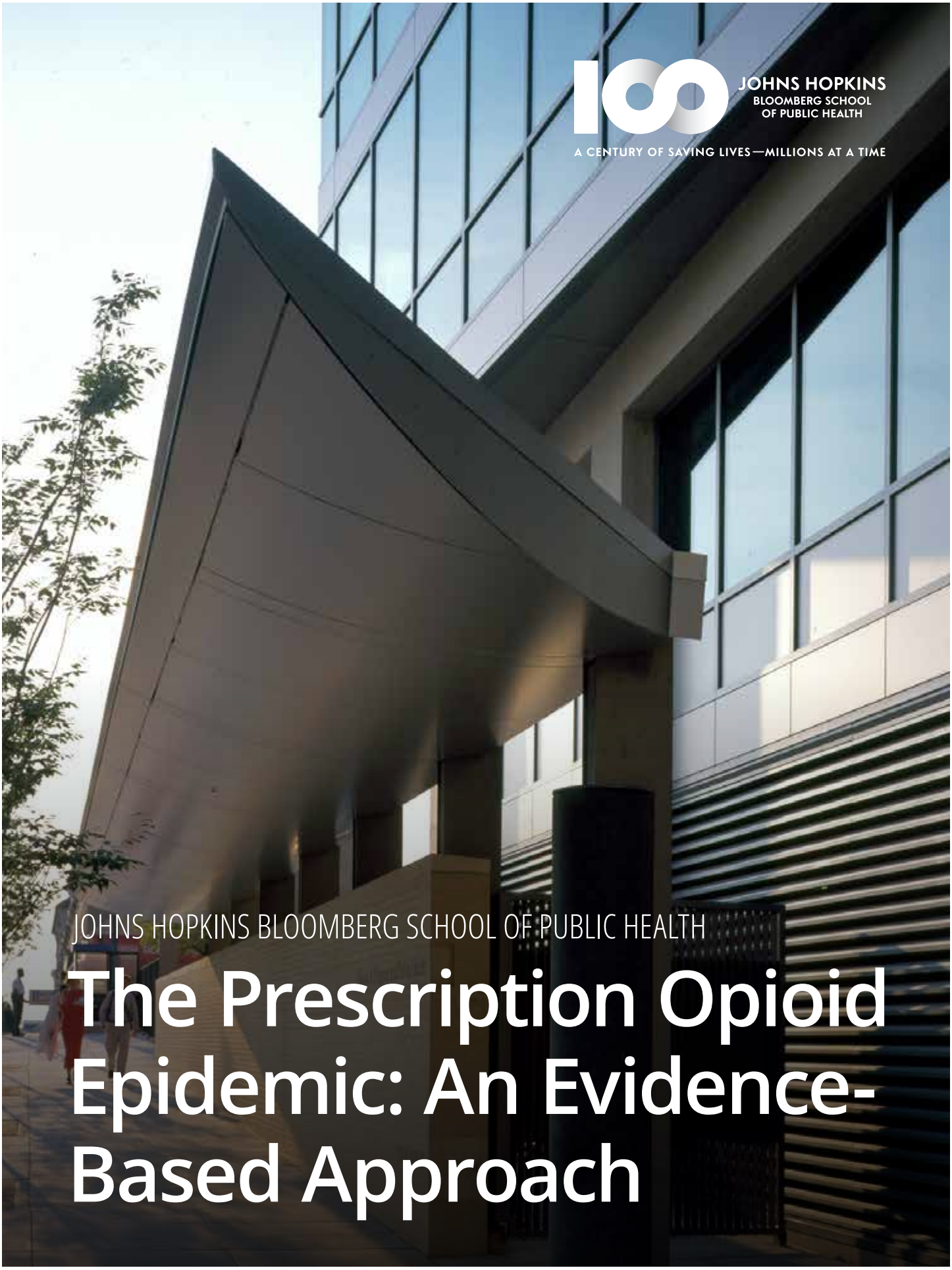

JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

The Prescription Opioid Epidemic: An Evidence-Based Approach

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#4 ENGINEERING STRATEGIES: PRESCRIPTION DRUGS AND PACKAGING

STATEMENT OF THE PROBLEM

Although prescription drug abuse is a complex, multi-faceted issue, the data strongly indicate that the vast majority of prescription drugs that are abused come from legitimate prescriptions.[95] However, once they are dispensed, prescription drugs are frequently diverted to people using them for nonmedical purposes.[96] Indeed, approximately 70 percent of people who report nonmedical use of prescription opioid pain relievers state they got their most recently used drug from a friend or family member.[97] One component of a comprehensive approach to the problem is to leverage engineering strategies to inform the development of innovative packaging for prescription drug dispensing that can reduce nonmedical use and diversion.

The concept of engineering solutions to improve product safety is a cornerstone of injury prevention. Research indicates that changing products to make them safer is often more effective at reducing injury and death compared to trying to change personal behaviors.[98] Successful examples that have resulted in reductions in morbidity and mortality include the introduction of child-resistant caps to reduce pediatric poisonings; and reductions in motor vehicle crash deaths after mandatory implementation of collapsible steering wheels, energy-absorbing vehicle frames and other physical modifications to motor vehicles.[99, 100, 101, 102] These product-oriented approaches can serve as a model for engineering solutions for prescription drug abuse.

SYNTHESIS OF AVAILABLE EVIDENCE

The U.S. Food and Drug Administration (FDA) highlighted the potential for innovative packaging solutions to be a part of the Agency's response to prescription drug abuse when it published a notice for public comment in the Federal Register in April 2014. The FDA stated that designs for drug packaging have evolved significantly in the past decade and now include many technology-based features — such as electronic systems for monitoring, accessing and improving adherence to medication regimens — that also could help to prevent prescription drug abuse and diversion. Examples of design strategies mentioned by the FDA include: systems that remind patients to take a dose, track when a dose is taken, and limit further access until the next dose is due; radio-frequency identification-based systems; and microchips embedded within tablets. Often these technologies are packaged with data capture systems to provide feedback to providers on adherence, use and potentially tampering.[103]

Although most prescription drug packaging solutions have been designed to improve medication compliance among patients using non-controlled substances for chronic conditions [104, 105,] these solutions could be adapted to help prevent prescription drug abuse and diversion. For example, these products could reduce serious complications such as overdose by facilitating appropriate dosage and administration, and could help providers monitor for signs of abuse or diversion. In addition, products that limit access to the medication during non-dosing periods could help prevent use of the medication by someone for whom it was not prescribed. The concept of personalization, i.e., use of a personal identification number, radio-frequency device, fingerprint or other biometrics, has been proposed to prevent other types of injuries [106] and could be applied to prescription drug packaging as well. An example is a pill dispenser that requires a specific fingerprint before releasing the appropriate pain medication at the appropriate time.

Data on the effectiveness of packaging designs on prescription drug abuse is limited. One study of 37 individuals assessed the impact of an electronic medicine dispenser on diversion of buprenorphine-naloxone among patients receiving the drug for opioid addiction treatment. The researchers found 68 percent of patients preferred to use the electronic dispenser to store their tablets compared to the traditional prescription container; 16 percent stated that the dispenser had prevented them from diverting their buprenorphine; 23 percent stated the dispenser prevented others from diverting their buprenorphine; and 58 percent believed the dispenser could prevent diversion. Additionally, 19 percent stated that it was difficult to tamper with the dispenser and 58 percent stated it was impossible to tamper with the dispenser.[107] Another product, which couples a flow-controlled, tamper-resistant medication dispenser with a Web and phone accessible treatment portal, has demonstrated sufficient promise to obtain funding from the National Institute on Drug Abuse. A phase II randomized controlled trial will assess use of the device and opioid misuse among patients from two pain management clinics.[108] However, results from this trial were not available as of June 2015.

A review of the currently available and in-development opioid packaging designs by Lehigh University concluded that many of the commercialized technologies such as locking caps, tamperproof packages and pill-dispensing products are most likely to deter unintentional misuse by elderly people or children and have limited abilities to prevent intentional abuse. However, newer technologies, such as radio-frequency identification wireless technologies and simple technologies combined with radio-frequency identification — as well as other types of smart technologies — have the potential to play a role in deterring intentional opioid abuse by increasing communication between healthcare professionals and patients.[109] As part of their senior mechanical

engineering design course, students at Johns Hopkins University successfully created a prototype of a new design that is tamper-resistant, personalized with fingerprint technology and programmed to deliver a one-month supply of an opioid in the right time and dosage. Only a pharmacist would be able to open and lock the device.[110]
Despite the very limited data on effectiveness, there are a number of products currently being marketed to consumers. There is a pressing need for research to understand the impact of these products on prescription drug abuse. In addition to research questions on effectiveness, there are a number of outstanding questions that need to be explored before widespread adoption of these products can occur. These questions include:

- Where will these products enter the medication prescribing and use process? Will they be made available for purchase by patients for use in their homes? Will pharmacists use them instead of traditional pharmacy dispensing vials? Will manufacturers move away from bulk product distribution and incorporate these packaging designs for direct dispensing from the doctor's office or pharmacy?
- How will these products be regulated? As consumer products? As medical devices? As a combination drug-device?
- Who will take on the costs for these products? Pharmacies? Patients? Insurers/PBMs?
- Who will control, monitor and have access to the data available from these devices?

RECOMMENDATIONS FOR ACTION

4.1 CONVENE A STAKEHOLDER MEETING.

Work with the FDA to convene a meeting with product developers and key stakeholders to assess the current product environment (e.g., products available, evidence to support effectiveness, regulatory issues) and identify high priority future directions for engineering-related solutions.

Rationale: Engineering solutions to deter nonmedical use of prescription opioids are promising and under development. There is a need for coordination of and support for the current efforts to ensure this line of innovation is adequately supported, quickly brought to market and rigorously evaluated.

Current Status: There is no national organizing effort underway; the FDA could promulgate rules or guidance to industry that will affect these innovations and the FDA is a logical stakeholder to convene a meeting or to serve as a partner to convene such a meeting.

4.2 SPONSOR DESIGN COMPETITIONS.

Partner with stakeholders to develop design competitions to incentivize innovative packaging and dispensing solutions.

Rationale: Design competitions have been used to encourage and support innovation in many areas. Engineering strategies for prescription packaging are a logical candidate for such a competition.

Current Status: We are unaware of any design competitions on this subject.

4.3 SECURE FUNDING FOR RESEARCH TO ASSESS THE EFFECTIVENESS OF INNOVATIVE PACKAGING AND DESIGNS AVAILABLE AND UNDER DEVELOPMENT.

Rationale: Data on the effectiveness of packaging interventions is limited. Research is needed to evaluate the engineering innovations under development and to inform future development.

Current Status: We are unaware of any funding source dedicated to evaluating engineering designs for prescription packaging.

4.4 USE RESEARCH TO ENSURE PRODUCT UPTAKE.

Engage with key stakeholders, such as product developers, drug manufacturers, pharmacies, payers, regulators, chronic opioid therapy patients and the public to explore potential barriers and incentives to product uptake, including a tiered reimbursement structure based on packaging designs with demonstrated effectiveness.
Rationale: Innovations in prescription packaging are promising, but little is known about how to ensure the public will use these products and that the products will be integrated into existing payment policies. Research is needed to ensure that these aspects of translation are understood.

Current Status: We are unaware of any efforts to gather empirical data about how to ensure innovative engineering packaging for prescriptions is effectively integrated into the consumer market.