Innovations in Abuse-Deterrent Pharmaceutical Packaging

Preventing medication misuse and addiction on the home front.



SCOPE OF THIS WHITE PAPER

The intent of this white paper is to:

- **1.** Review the United States opioid epidemic.
- 2. Review current approaches towards preventing and mitigating the opioid epidemic.
- **3.** Discuss abuse-deterrent packaging as a way to prevent the misuse of or accidental access to opioids or other powerful medications.

THE PROBLEM

The United States is in the grips of an opioid epidemic taking a tragic toll on many fronts. Families are torn apart and communities struggle. Hospital and social systems are fraying. The judicial and penal systems are overwhelmed as crime escalates. And overdose deaths continue to soar.

Over the past two decades, the use of opioids (man-made opiates) has escalated dramatically within the United States.

- Between 1999 and 2014, the amount of prescription opioids sold in the U.S. nearly quadrupled.
- In 2015, an estimated 828,000 people aged 12 years or older used heroin in the United States and over 12 million people misused prescription opioids.²

In the United States, where approximately one quarter of estimated global drug-related deaths are recorded, overdose deaths continue to rise.³

- Between 2012 and 2015, overdose deaths from synthetic opioids (other than methadone) increased by 265 percent, and between 2014 and 2015 by 72 percent.⁴
- Drug overdose is now the number one cause of accidental death in the U.S. In 2014, approximately 129 people in the United States died every day from overdose—which means that more people died from overdose than from motor vehicle crashes.⁵ More than 6 out of 10 overdose deaths involved opioids.⁶

Overdose Death Rates 1999 2015 Deaths per 100,000 0-8 8.1-18 18.1-28 Designed by L. Rossen, B. Bastian, & Y. Chong

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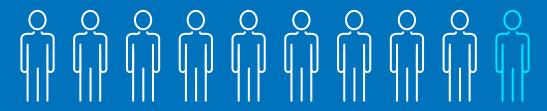
Source: CDC/NCHS, National Vital Statistics System



OPIOIDS, YOUTH, AND CHILDREN

In 2014, the Centers for Disease Control and Prevention (CDC) added prescription drug overdose prevention to its list of top five threats to public health. Adolescents, who test limits and feel invulnerable, are squarely in the crosshairs of pain pill misuse. The 2014 National Survey on Drug Use and Health indicated that opioid pain relievers were the second most common illicit drug use category among those aged 12 -17. (The most popular was marijuana.)⁷ In 2014, more than 1,700 young adults (aged 18-24) died from prescription drug overdoses (primarily opioids), and many more needed emergency treatment.⁸

According to the National Institute on Drug Abuse (NIDA), 6.5 million Americans aged 12 or older used prescription drugs non-medically in 2013.9 Drug use at an early age is an important predictor of the subsequent development of a Substance Use Disorder. The majority of those who have a Substance Use Disorder started using alcohol or other drugs before age 18 and developed their disorder by age 20.10



9 out of 10 people with substance abuse problems started using by age 18.

Source: https://www.centeronaddiction.org/addiction-prevention/teenage-addiction

The National Center on Addiction and Substance Abuse reports that 90% of all drug addiction starts in the teens. The significant increase in the number of opioid prescriptions in home medicine cabinets, coupled with a teen's natural curiosity and sense of invulnerability, puts an increased number of youth at risk for medication misuse today and the potential to develop Substance Use Disorder tomorrow.

Increasing rates of adult prescriptions are strongly associated with increases in drug exposures and poisonings among children.

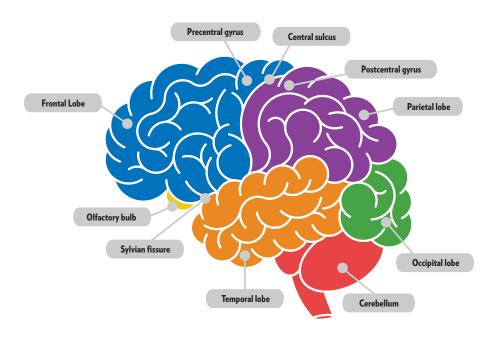
Young children also pay a price for our nation's dramatic increase in opioid prescriptions. Burghartt et al. demonstrated an association between adult prescription drug use and pediatric medication poisonings between 2000 and 2009, with the greatest risk for children under 6 years old. Among children this age who were hospitalized because of an unintentional ingestion, opioids were the most commonly implicated prescription medication.

As the accidental poisonings from opioids increases, so does the child death rate. A new analysis of state data on birth and death showed that accidental child poisonings, including those related to opioids, are also on the increase.¹³

DEFINITION OF ADDICTION AND DEPTHS OF THE OPIOID EPIDEMIC

NIDA defines addiction as "a chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences. It is considered a brain disease because drugs change the brain; they change its structure and how it works. These brain changes can be long lasting and can lead to many harmful, often self-destructive, behaviors."14 For many, addiction begins very innocently with a prescription from a doctor for injury or surgery. Data shows that the longer a patient takes prescription opioids, the more likely they are to become chemically-dependent upon their medication. In fact, the length of time a prescription covers is now considered a predictor of the likelihood of addiction developing.¹⁵

Addiction is a Brain Disease



And prescription medications can fall into the wrong hands, with curious teenagers pilfering a pill here or there from the family medicine cabinet. Depending upon their personal risk factors for addiction (e.g., family genetics, history of early childhood trauma, mental health issues), young people's brains - neurological "works in progress" - may become chemically-dependent upon opioids. In 2014, the non-medical use of prescription medications was highest among people aged 18 to 25.16

People who can no longer obtain the prescription opioids upon which they have become dependent often resort to the opioid they can find – heroin. The unpredictable purity of heroin, which may be diluted with fentanyl or even stronger opioids, plays a part in the substantial increase in mortality associated with opioid overdose. In some cases, the deadly opioid behind an overdose was a prescription medication; in other cases, the opioid was heroin, fentanyl or even carfentanil, a tranquilizer used to sedate elephants.

Prescription opioid misuse can be a killer even if it doesn't lead to overdose. A recent study showed prescription opioid misuse was associated with anywhere between a 40 and 60 percent increased risk for suicidal ideation (thoughts of suicide). Those reporting at least weekly opioid misuse were at much greater risk for suicide planning and attempts than those who used less often. They were about 75 percent more likely to make plans for a suicide and made suicide attempts at a rate 200 percent greater than those unaffected.¹⁷

As a footnote, it's important to be aware that opioid pain medications are not the only medications vulnerable to misuse or accidental poisonings. Anti-anxiety medications, stimulants, and other prescription medications may be pilfered from the medicine cabinet. Even vitamins can be poisonous to a curious toddler. Securing medications in abuse-deterrent packaging can keep toddlers and teens safe by preventing the accidental or illicit consumption of powerful medications.

THE OPIOID EPIDEMIC IN THE U.S.



people misused prescription opioids



2.1 million

people misused prescription opioids for the first time



2 million

people had prescription opioid use disorder



828,000

people used heroin



135,000

people used heroin for the first time



33,091

people died from overdosing on opioids



15,281

deaths attributed to overdosing on commonly prescribed opioids



9,580

deaths attributed to overdosing on synthetic opioids



12,989

deaths attributed to overdosing on heroin



\$78.5 billion

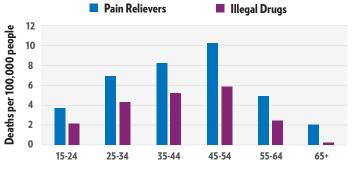
In economic costs (2013 data)

A STEEP CLIMB IN OPIOID USE AND ABUSE

The Surgeon General reports that opioid analgesic pain relievers are now the most prescribed class of medications in the United States, with more than 289 million prescriptions written each year. 18 Illustrating one type of "collateral damage," in Tennessee in 2015, 174 people died in crashes in which a driver either tested positive for drugs or an officer determined drugs contributed to the crash. That's an 89 percent increase in five years in the number of fatal crashes featuring a driver who was impaired by drugs.¹⁹



Deaths from Opioid Pain Relievers Exceed Those from All Illegal Drugs



Source: CDC, Morbidity and Mortality Weekly Report, 60(43): 1489, 2011

91 Americans die every day from an opioid overdose (including prescription opioids and heroin).

Centers for Disease Control - 2015

More people died from drug overdoses in 2014 than in any other recorded year.²⁰ and the dramatic rise in the rate of addiction shows no signs of slowing down.²¹

ROOT CAUSES OF THE OPIOID EPIDEMIC

Since ancient times, people have used opiates - beginning with the humble poppy - to manage pain or create euphoria. In the United States, the utilization of pain pills began to gain traction in the late '90 for a variety of key reasons:

- Unaware of the potential for chemical-dependency, doctors have prescribed highly addictive pain medications liberally. There is a direct correlation between the number of pills taken and the likelihood of developing dependence: Almost 30 percent of patients who take pain medications for 30 days will still be taking them one year later, often in increasing amounts.²²
- Parents and youth alike mistakenly believe that medications from a doctor are safe. And parents, unaware that addiction is an equal-opportunity brain disease that can strike in any neighborhood, believe "Not my family...not my kid." Parents are not monitoring their medications, and curious teens rarely see a risk in stealing a pill or two.²⁵ Pills are easy to come by: most adolescents and adults reporting recent non-medical use of opioid medications obtain these medications through their family or friends.²⁶



COSTS OF THE OPIOID EPIDEMIC

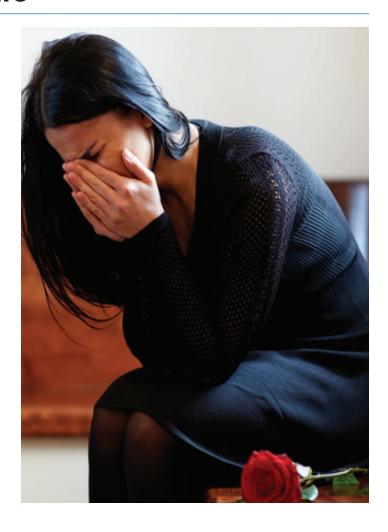
Considered by many to be the most pervasive and costly public health crisis facing our nation, addiction takes a heavy toll on communities and families alike. Burglaries, drugged driving, homicides, suicides, child abuse, sexual violence and assault often feature drug abuse as the root cause. Significant costs include incarceration, loss of jobs and the destruction of families.

Medical systems incur huge costs as they try to manage the tsunami of addicted babies born to addicted mothers. Social service agencies across the nation strain under the weight of caring for "opioid orphans." Drugs use also contributes to the development of other chronic diseases such as cardiovascular and cardiopulmonary diseases which take a toll on the quality of life, personal productivity and society.

The cost of losing a teenager to overdose or a toddler to accidental poisoning is impossible to calculate.

In 2015, two million people had a prescription opioid use disorder and 591,000 suffered from a heroin use disorder. The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse alone in the United States is \$78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement.²⁸ The cost of losing a teenager to overdose or a toddler to accidental poisoning is impossible to calculate.

The epidemic also poses a potential threat to the physical, mental and emotional well-being of the millions of Americans who suffer from chronic pain conditions such as rheumatoid arthritis. Their access to timely and legitimate medication may be imperiled by a groundswell of opposition to the use of opioids, even when appropriately prescribed and managed to treat debilitating pain.



Annual Economic Burden of Prescription Opioid Misuse in the U.S.



Source: U.S. Centers for Disease Control and Prevention, 2013 Estimated Costs

COMPLEX PROBLEMS CALL FOR COMPREHENSIVE SOLUTIONS

Because the opioid epidemic is not caused by a single driver, prevention and mitigation efforts must take place on multiple fronts including:

- Hospital systems that educate doctors and patients about the benefits, risks and alternatives to opioid medication.
- Doctors who are writing fewer opioid prescriptions for prescriptions that are shorter in duration.
- Community prevention coalitions that are educating and engaging every facet of their community (e.g., schools, parents, merchants, medical providers, houses of faith) in community-wide awareness and prevention activities.
- Existing medications that are being reformulated to make them less abusable (i.e., more difficult to crush or dissolve for injection or nasal ingestion.)
- New medications that are being developed to manage pain without the reward-enhancing and respiratory-depressing effects of opioids.
- The DEA's twice-yearly drug take-back days where people can safely dispose of excess medications.
- Community facilities, such as libraries and high schools that are being equipped with overdose-reversing naloxone nasal sprays or injections.
- Abuse-deterrent packaging that prevents the pilfering or accidental ingestion of dangerous medications.

PREVENTION IS AN ESSENTIAL PART OF THE SOLUTION

Data reveals the impact of effective prevention techniques. In 2015 alone, the use of seat belts in passenger vehicles saved an estimated 13,941 lives of occupants aged five and older, and frontal air bags saved an estimated 2,573 lives of car occupants aged 13 and older.²⁹ Prevention work on the tobacco and HIV fronts have reduced the incidence of those deadly diseases, and prevention efforts have helped reduce the incidence of many cancers, including cervical cancer.³⁰ The gains from each of these prevention efforts continue to grow over time.

Every dollar invested in prevention programs yields a ten-fold savings in addiction costs.

Evidence shows that when we invest in prevention, we can save lives as well as spare budgets. Research shows that every dollar invested in research-based prevention programs yields a ten-fold savings vis-a-vis treatment for alcohol or other substance misuse-related costs.³¹ Spending \$1,000 on effective prevention efforts, for example, avoids an estimated cost of \$10,000 to manage the consequences of drug misuse or abuse.

ABUSE-DETERRENT PACKAGING AS A PREVENTION TOOL

The United States Congress passed the Poison Prevention Packaging Act of 1970 in the wake of a history of accidents involving children who had opened household packaging and ingested the contents. This gave the U.S. Consumer Product Safety Commission the authority to regulate this area, which represents a major policy success. 32 A study of child-resistant packaging over the first twenty years of use concluded that child resistant packaging reduced mortality by over 45%.³³

Professional groups and organizations endorse education messages that support locking up or latching medicines and other household products implicated in pediatric poisonings. Distributing cabinet latches and advising parents to lock up medications has increased poison prevention practices in households with children.³⁴



Child-resistant packaging exists beyond the pharmaceutical arena. For example, the manufacturer of Tide laundry detergent has introduced the Tide PODS® Child-Guard™ Pack with a Child-Guard™ Zipper that makes it harder for kids to get their hands on a colorful laundry pod that looks like candy or a toy.

Abuse-deterrent packaging impedes access to dangerous medications by physically preventing abusers from snitching one or two pills without detection. Psychologically, the mere use of abuse-deterrent packaging signals to parents and potential abusers that the medications are powerful and should be taken only as directed by the doctor. And if the packaging is tampered with or disappears entirely, it is evident to all that a problem exists.

> **Child-resistant packaging reduced** mortality by over 45%.

AN INNOVATIVE ABUSE-DETERRENT PACKAGING SOLUTION

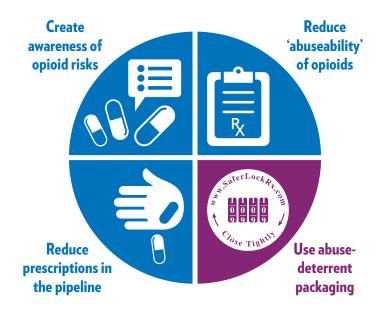
The Safer Lock™ is an innovative abuse-deterrent packaging solution that can help prevent medication misuse before it starts. Safer Lock is a four-digit combination locking cap (with 10,000 possible combinations) designed to prevent unauthorized access to prescription medication. The Safer Lock cap fits a wide variety of standard prescription bottles. Patients set the combination to their personal preference, and it cannot be opened or changed without being set for the correct current combination. If the bottle shows signs of tampering, it sets the stage for discussion and action within the household.



RECOMMENDATIONS

Creating awareness of the risks implicit in opioids, reducing the number of prescriptions in the pipeline, reducing the abusability of those prescription, and offering abuse-deterrent packaging are all facets of the complex strategy necessary to combat our nation's opioid epidemic. Potentially, the Poison Prevention Packaging Act of 1970 could be fortified to require higher standards of packaging on the substances deemed to be often abused or most deadly when accidentally ingested.

While research is required to evaluate how and where abuse-deterrent packaging can have the greatest impact on medication misuse and abuse, and accidental poisoning, we can take action now. A recent study showed that opioid pain reliever storage is less than ideal in households with children and adolescents, even though parents knew opioids were potentially dangerous, and at the same time, reported very few impediments to safely securing them.³⁵



Communication then holds one key to prevention: Research suggests that we may reduce risks by reducing the sheer number of opioid prescriptions and widely communicating clear recommendations on their safe storage and disposal to both the public and prescribers.³⁶

And access to abuse-deterrent products is another critical key. Let's follow the lead of safety product research that shows how making safety products and storage devices available is an effective way to increase their use.³⁷ While the cited research evaluates the impact of providing safety products in clinic or hospital-based safety resource centers, the study has broad implications: The two-fold key to safety product success is to communicate the need for safe medication storage while making it easy for the public to obtain abuse-deterrent devices.

References

- 1. Centers for Disease Control and Prevention. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2016. http://www.wonder.cdc.gov.
- 2. Quoted from the United States Substance Abuse and Mental Health Services Administration 2015 National Survey on Drug Use and Health: Misuse of prescription drugs was "redefined in 2015 as use in any way not directed by a doctor, including use without a prescription of one's own medication; use in greater amounts, more often, or longer than told to take a drug; or use in any other way not directed by a doctor." https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm
- 3. Rudd, Rose, Puja Seth, PhD1; Felicita David, MS1; Lawrence Scholl, "Increases in Drug and Opioid-Involved Overdose Deaths: United States, 2010-2015." 2016. Morbidity and Mortality Weekly Report, 65 (50 and 51):1445-1452. https://www.cdc.gov/mmwr/volumes/65/wr/mm655051e1_w
- 4. Rudd, Rose, Puja Seth, PhD1; Felicita David, MS1; Lawrence Scholl, "Increases in Drug and Opioid-Involved Overdose Deaths: United States, 2010-2015." 2016. Morbidity and Mortality Weekly Report, 65 (50 and 51):1445-1452. https://www.cdc.gov/mmwr/volumes/65/wr/mm655051e1.htm?s_cid=mm655051e1_w
- 5. Rudd, Rose, Noah Aleshire, Jon E. Zibbell, and R. Matthew Gladden, "Increases in Drug and Opioid Overdose Deaths United States, 2000–2014." Morbidity and Mortality Weekly Report, 64 (50);1378-82. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm
- Rudd, Rose, Noah Aleshire, Jon E. Zibbell, and R. Matthew Gladden, "Increases in Drug and Opioid Overdose Deaths United States, 2000–2014." Morbidity and Mortality Weekly Report, 64 (50):1378-82. https://www.cdc.gov/mmwr/breview/mww/breview/mww/brevi
- 7. 2104 National Survey on Drug Use and Health. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2014/N
- 8. Centers for Disease Control and Prevention. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2016. http://wonder.cdc.gov
- 9. National Institute of Drug Abuse. (2015). Drug Facts: Prescription and Over-the-Counter Medications. Bethesda, MD: National Institute of Drug Abuse. http://www.drugabuse.gov/publications/drugfacts/prescription-over-counter-medications.
- 10. Dennis, M.; TF Babor, C Roebuck; and J Donaldson. "Changing the focus: The case for recognizing and treating cannabis use disorders." Addiction 97:(51):4–15, 2002. https://www.ncbi.nlm.nih.gov/pubmed/12460125
- 11. Burghardt LC, JW Ayers, JS Brownstein, AC Bronstein, EB Ewald, FT Bourgeois. "Adult prescription drug use and pediatric medication exposures and poisonings." Pediatrics 2013; 132 (1): 18-27 http://pediatrics.aappublications.org/content/early/2013/05/29/peds.2012-2978
- 12. Lovegrove, Maribeth, J Mathew, C Hampp, L Governale, DK Wysowoscki, DS Budnitz. "Emergency hospitalization for unsupervised prescription medication ingestions by young children." Pediatrics. 2014; 143 (4). http://pediatrics.aappublications.org/content/early/2014/09/09/peds.2014-0840
- 13. Murphy, Sherry L, T. J. Mathews, Joyce A. Martin, Cynthia S. Minkovitz, Donna M. Strobino. Annual Summary of Vital Statistics: 2013-2014, American Academy of Pediatrics. March 21, 2017. http://pediatrics.aappublications.org/content/early/2017/05/26/peds.2016-3239
- 14. National Institute on Drug Abuse, "The Science of Drug Abuse and Addiction: The Basics." Media Guide. www.drugabuse.gov/publications/media-guide/science-drug-abuse-addiction-basics.
- 15. Shah, Anuj, Corey J. Hayes, Bradley C. Martin, "Characteristics of initial prescription episodes and likelihood of long-term opioid use United States, 2006–2015," 2017. Morbidity and Mortality Weekly Report, 66 (10);265–269. https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm
- 16. 2104 National Survey on Drug Use and Health. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2014/
- 17. Ashrafioun, Lisham, TM Bishop, KR Conner. WR Pigeon, "Frequency of prescription opioid misuse and suicidal ideation, planning, and attempts," Journal of Psychiatric Research 92 (2017); 1-7. http://www.journalofpsychiatricresearch.com/article/S0022-3956(16)30183-2/fulltext
- 18. U.S. Department of Health & Human Services, Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs and Health, 2016 (p 1-14). https://addiction.surgeongeneral.gov/
- 19. Mike Reicher, "Drugged driving overtakes alcohol in Tennessee road deaths," The Tennessean, September 29, 2016. http://www.tennessean.com/story/news/local/2016/09/28/drugged-driving-overtakes-alcohol-tennessee-road-deaths/90755050/
- 20. Understanding the Epidemic. Centers for Disease Control and Prevention. https://www.cdc.gov/drugoverdose/epidemic/index.html
- 21. Centers for Disease Control and Prevention/National Vital Statistics System. Number and age-adjusted rates of drug-poisoning deaths involving opioid analgesics and heroin: United States, 2000-2014. http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014
- 22. Shah, Anuj, Corey J. Hayes, Bradley C. Martin, "Characteristics of initial prescription episodes and likelihood of long-term opioid use United States, 2006–2015," 2017. Morbidity and Mortality Weekly Report, 66 (10); 265–269. https://www.cdc.gov/mmwr/volumes/66/wr/mm6610a1.htm
- 23. State of Ohio v. Perdue Pharma, Inc., 2017. http://www.ohioattorneygeneral.gov/Files/Briefing-Room/News-Releases/Consumer-Protection/2017-05-31-Final-Complaint-with-Sig-Page.aspx
- 24. Scott Higham and Lenny Bernstein, "Cherokee nation sues drug firms, retailers for flooding communities with opioids," Washington Post, April 20, 2017. https://www.washingtonpost.com/investigations/cherokee-nation-sues-drug-firms-retailers-for-flooding-communities-with-opioids/2017/04/20/03d04a74-2519-11e7-b503-9d616bd5a305_story.html?utm_term=.8463098484f8
- 25. Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health: mental health findings. http://www.samhsa.gov/data/sites/default/files/NSDUHmhfr2013
- 26. National Institute of Drug Abuse. (2015). Drug Facts: Prescription and Over-the-Counter Medications. Bethesda, MD: National Institute of Drug Abuse. http://www.drugabuse.gov/publications/drugfacts/prescription-over-counter-medications
- 27. Degenhardt, Louisa. and Wayne Hall. "Extent of illicit drug use and dependence, and their contribution to the global burden of disease." (2012) The Lancet, 379, 55-70. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61138-0/abstract
- 28. National Institute of Drug Abuse. (2015). Drug Facts: Prescription and Over-the-Counter Medications. Bethesda, MD: National Institute of Drug Abuse. http://www.drugabuse.gov/publications/drugfacts/prescription-over-counter-medications
- 29. US Department of Transportation, Traffic Safety Facts, August 2016. https://crashstats.nhtsa.dot.gov/Api/Public/ViewPublication/812319
- 30. The Power of Prevention. Centers for Disease Control and Prevention, 2009. https://www.cdc.gov/chronicdisease/pdf/2009-power-of-prevention.pdf
- 31. Aos, Steve., Polly. Phipps, Robert Barnoski, & Roxanne. Lieb. (2001). The comparative costs and benefits of programs to reduce crime. Version 4.0. Olympia, WA: Washington State Institute for Public Policy. http://www.wsipp.wa.gov/Reports/01-05-1201
 - Pentz, M. A. (1998). Costs, benefits, and cost-effectiveness of comprehensive drug abuse prevention. In W. J. Bukoski & R. I. Evans (Eds.), Cost-benefit/cost-effectiveness research of drug abuse prevention: Implications for programming and policy. NIDA Research Monograph No. 176.(pp. 111-129). Washington, DC: U.S. Government Printing Office. https://archives.drugabuse.gov/pdf/monographs/monograph176/monograph176.pdf
- 32. The Power of Prevention. Centers for Disease Control and Prevention, 2009. https://www.cdc.gov/chronicdisease/pdf/2009-power-of-prevention.pdf
- 33. Rodgers, Gregory, "The safety impacts of child-resistant packaging for oral prescription drugs," The Journal of the American Medical Association, June, 1996. Volume 274 http://citeseerx.ist.psu.edu/viewdoc/download?-doi=10.1.1.507.3265&rep=rep1&type=pdf
- 34. Archana FA, Sutton AJ, Kendrick D et al. "The effectiveness of different interventions to promote poison prevention behaviours in households with children; a network meta-analysis." PLoS One 2015; 10(3): e0121122. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4404249/
- 35. Eileen M. McDonald, Alene Kennedy-Hendricks, Emma E. McGinty, Wendy C. Shields, Colleen L. Barry, Andrea C. Gielen. "Safe storage of opioid pain relievers among adults living in households with children." Pediatrics. 2017;139(3):e20162161. http://pediatrics.aappublications.org/content/early/2017/02/16/peds.2016-2161
- 36. Gielen, AC, EM McDonald, ME Wilson, et.al. "Effects of improved access to safety counseling, products, and home visits on parents' safety practices: result of a randomized trial." Archives of Pediatric Adolescent Medicine. 2002. 156(1): 33-40. http://jamanetwork.com/journals/jamapediatrics/fullarticle/191435
- 37. Gielen et al. "Effects of improved access to safety counseling, products, and home visits on parents' safety practices: result of a randomized trial." Archives of Pediatric Adolescent Medicine. 2002. 156(1): 33-40. http://imanetwork.com/journals/jamapediatrics/fullarticle/191435

