

FDA's Actions to Address the Opioid Epidemic

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CBI Abuse-Deterrent Formulation
Summit

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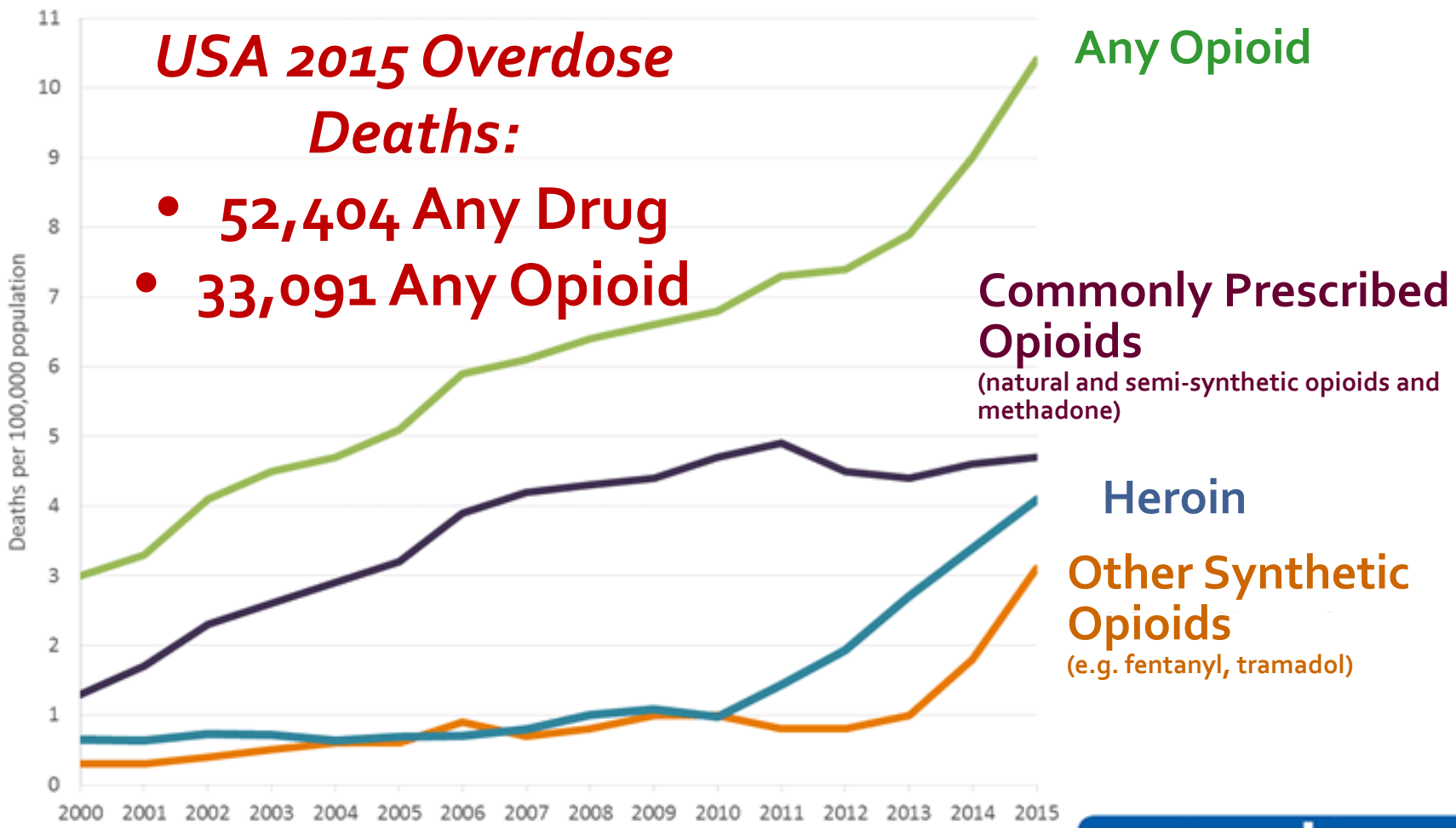
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Overall Messages

- The FDA work to improve the safe use of opioids is taking place within a larger policy framework aimed at addressing opioid abuse while assuring appropriate access to effective pain treatment
- Ongoing and planned activities reflect the commitment by FDA to use of all of our available tools to appropriately manage pain while also addressing the opioids crisis

Marked *Increases in Prescription Opioid and Heroin Overdose Deaths* in the USA 2000 to 2015

Overdose Deaths Involving Opioids, United States, 2000-2015



USA 2015 Overdose Deaths:

- 52,404 Any Drug
- 33,091 Any Opioid

Any Opioid

Commonly Prescribed Opioids
(natural and semi-synthetic opioids and methadone)

Heroin

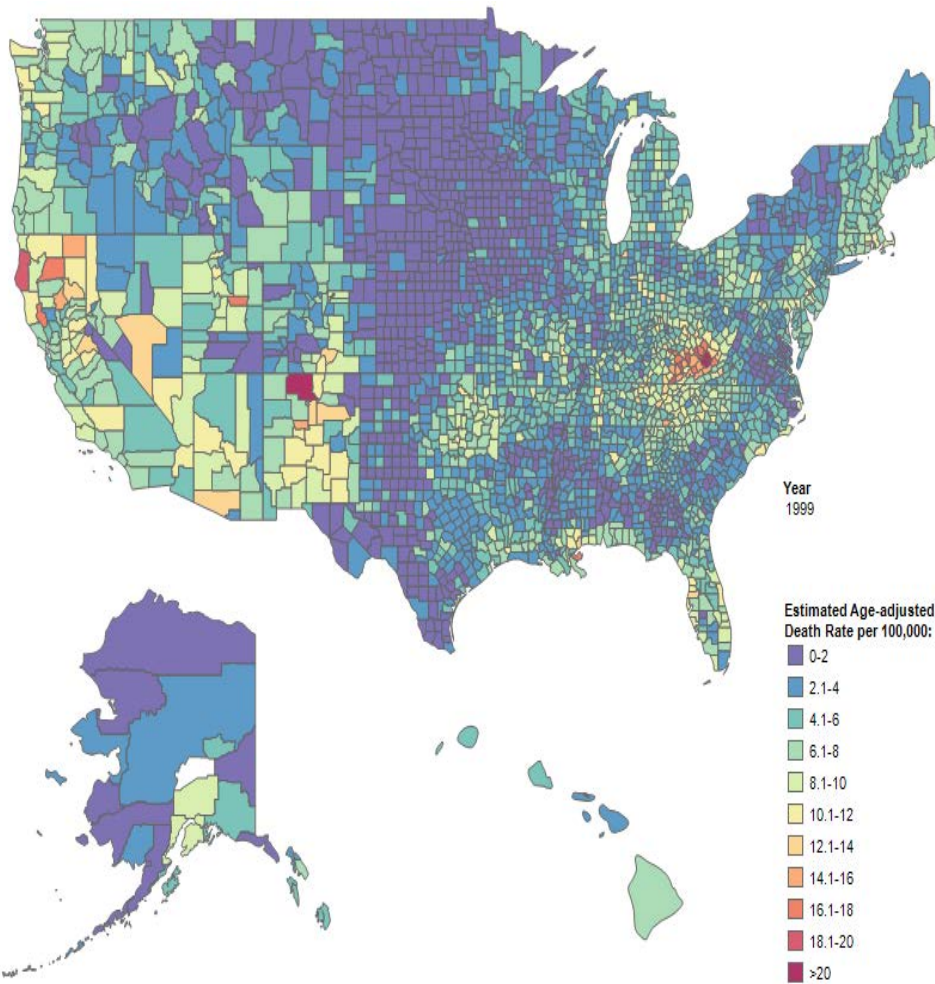
Other Synthetic Opioids
(e.g. fentanyl, tramadol)

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://wonder.cdc.gov/>.

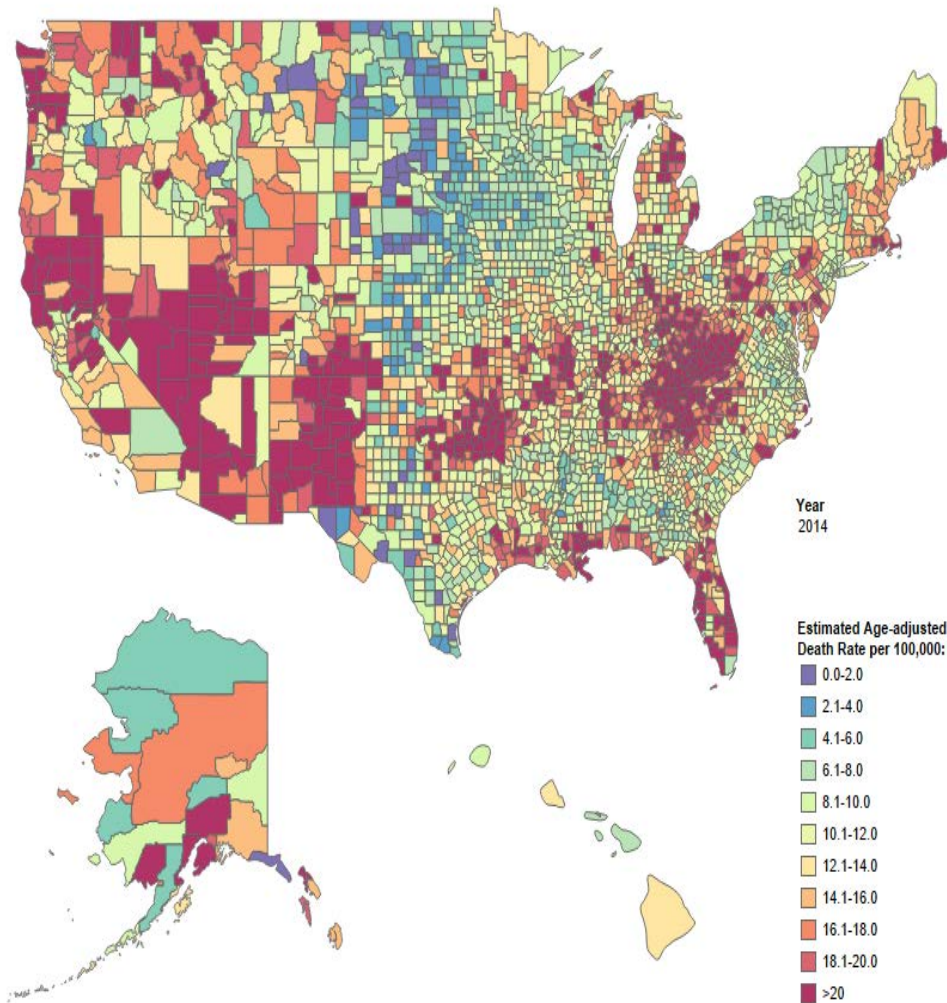


Overdose Death Rates

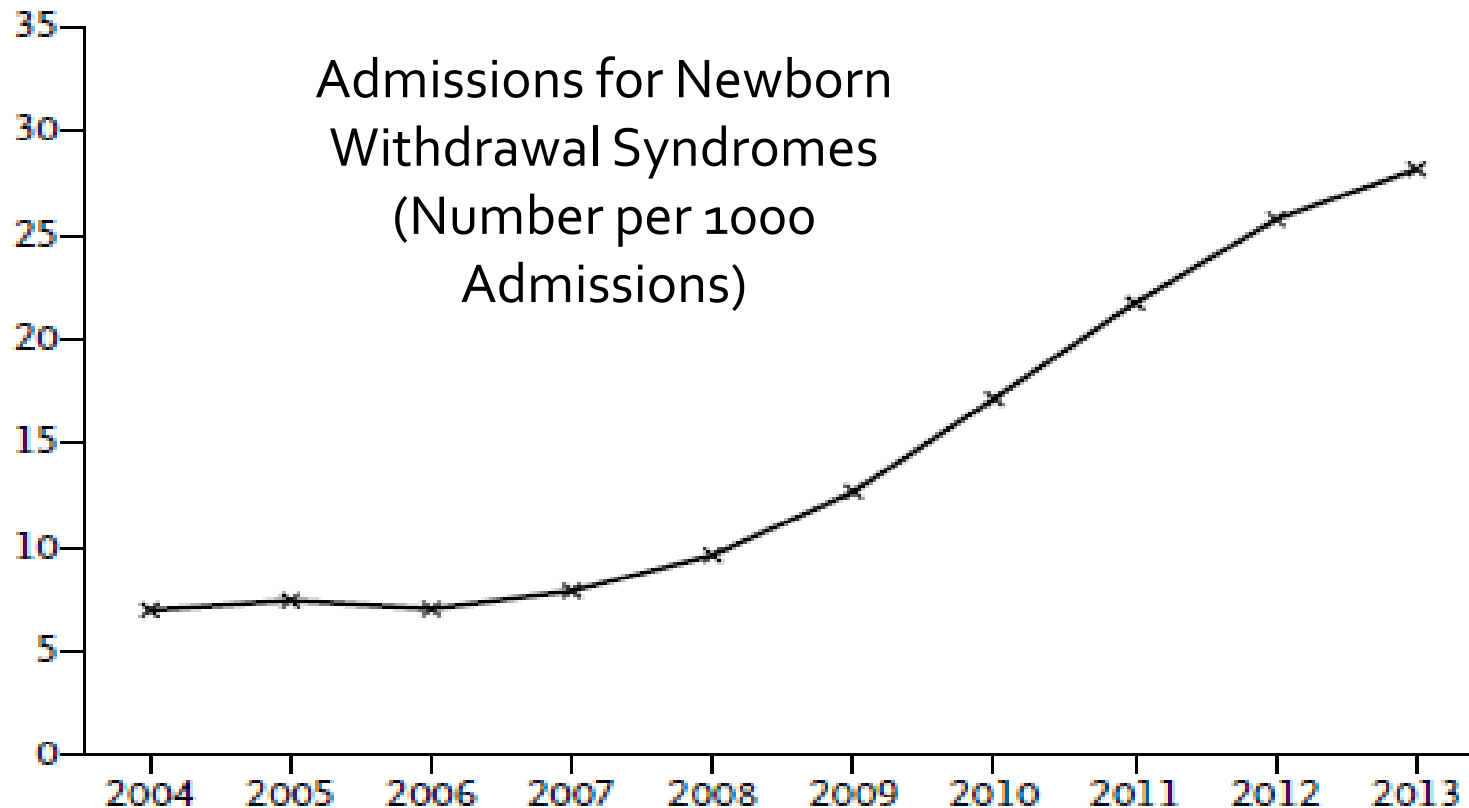
1999



2014



Impact of Crisis: Increasing Prenatal Exposure



Impact of Crisis: Infectious Disease Transmission

HIV and Hepatitis C Outbreak Linked to Oxycodone Injection Use in Indiana, 2015

Centers for Disease Control and Prevention

MMWR

Early Release / Vol. 64

Morbidity and Mortality Weekly Report

April 24, 2015

Peters et al.

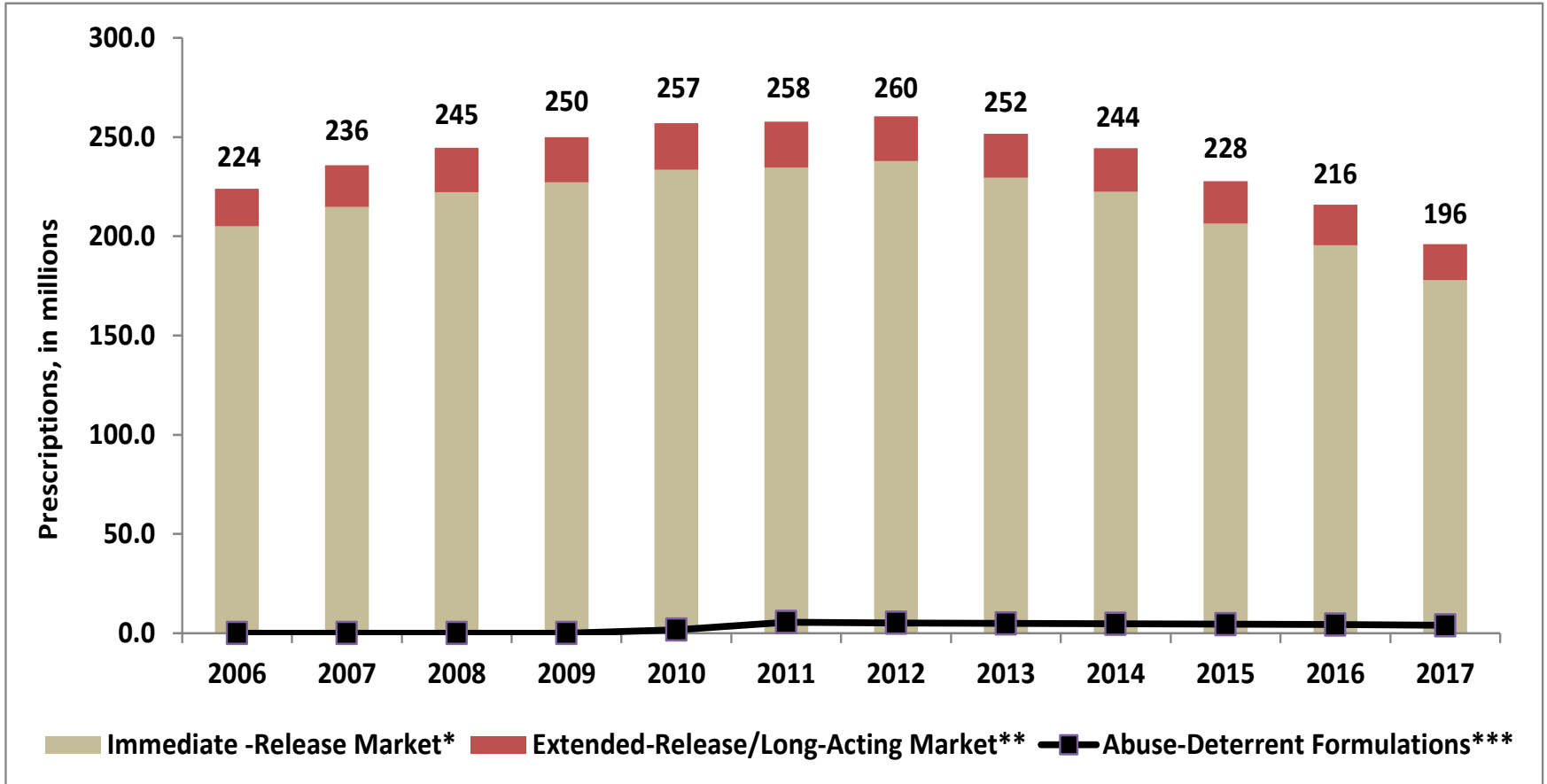
The New England Journal of Medicine

2016;375:229-239

U.S. Prescribing Rates - Trends

- U.S. prescribing rates peaked in 2012 at 81.3 prescriptions per 100 persons¹¹
 - Total: 255 million prescriptions
- Opioid prescribing has been decreasing between 2012 and 2016.
- U.S. prescribing rate in 2016 was 66.5 prescriptions per 100 people
 - 214 million prescriptions
- Rates continue to vary widely
 - Some counties had rates 7 times the national average

Nationally Estimated Number of Prescriptions Dispensed for Opioid Analgesics Products from U.S. Outpatient Retail Pharmacies



Source: IQVIA, National Prescription Audit (NPA) and static data 2006-2011. January 2006-December 2017.

Static data extracted March 2017 and 2012-2017 data extracted February 2018.

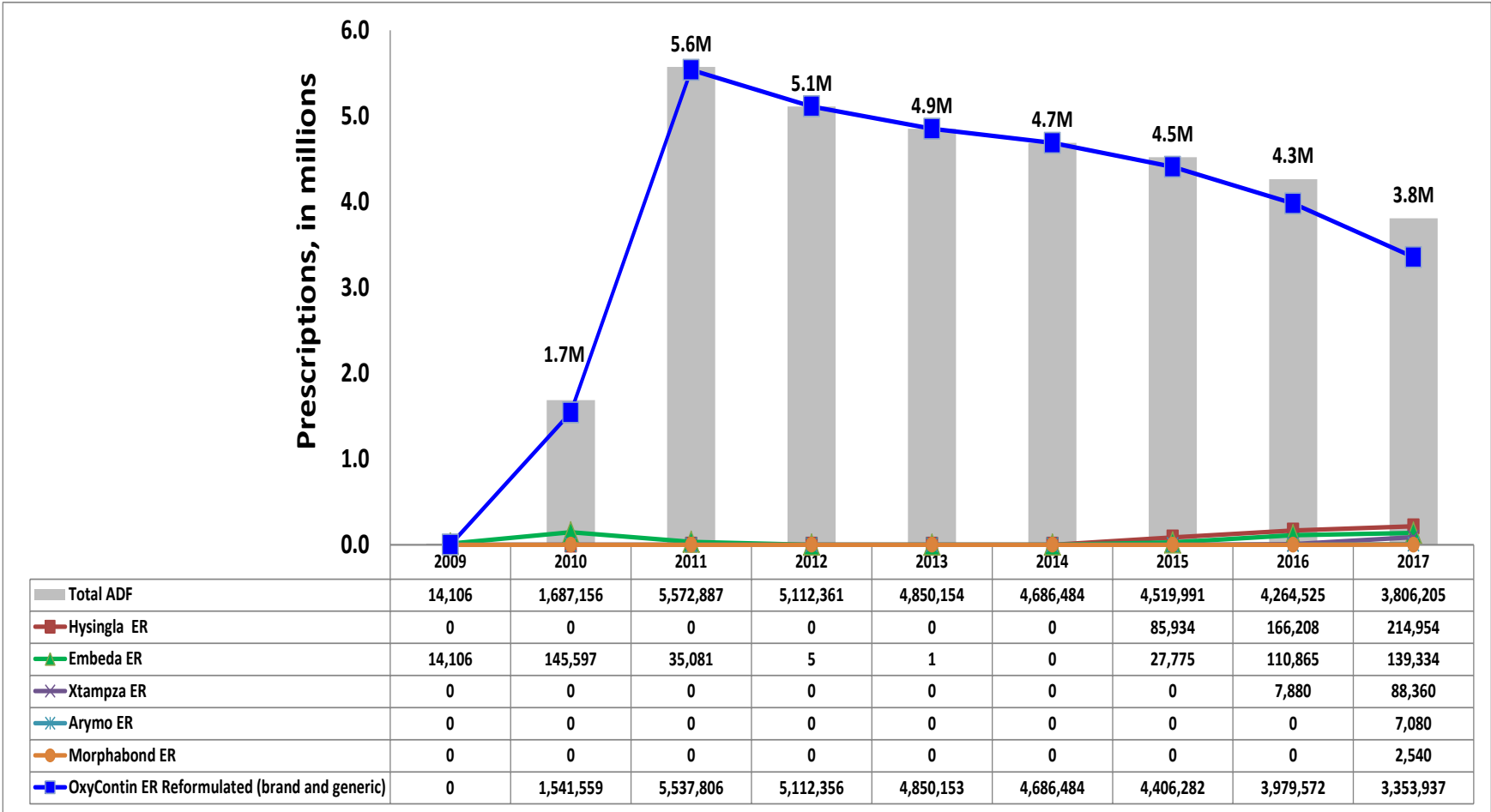
*Immediate-Release formulations include oral solids, oral liquids, rectal, nasal, and transmucosal

**Extended-Release/Long-Acting formulations include oral solids and transdermal patches

***Abuse-deterrent formulation opioid products include Arymo ER, Embeda ER, Hysingla ER, Morphabond ER, Xtampza ER, OxyContin ER Reformulated (Approval in April 2010)

Note: Include opioid analgesics only, excluding injectable formulations as well as opioid-containing cough-cold products and opioid-containing medication-assisted treatment (MAT) products

Nationally Estimated Number of Prescriptions Dispensed for Abuse-Deterrent Formulation (ADF) Opioid Analgesic Products* from U.S. Outpatient Retail Pharmacies



Source: IQVIA, National Prescription Audit™, Years 2009-2017. Data Extracted February 2018.

*ADF Products not marketed during study period: RoxyBond (Oxycodone IR) - Approved 04/2017; Targiniq ER (oxycodone/naloxone ER) - Approved 07/2014; Troxyca ER (Oxycodone/naltrexone ER) - Approved 08/2016; Vantrela ER (Hydrocodone ER) - Approved 01/2017

Equally Critical Social and Medical Issue: Pain in America

- From the Functioning and Disability Supplement of the 2012 National Health Interview Survey
 - 126.1 million adults reported some pain in the previous 3 months
 - 25.3 million adults (11.2%) suffering from daily (chronic) pain
 - 23.4 million (10.3%) reporting a lot of pain.
 - Based on the persistence and bothersomeness of their pain, 14.4 million adults (6.4%) were classified as having the highest level of pain, category 4, with an additional 25.4 million adults (11.3%) experiencing category 3 pain.

Pain in America (cont)

- Treatment options for pain: pharmacologic, physical medicine, behavioral medicine, neuromodulation, interventional, and surgical
- Optimal patient outcomes often result from a comprehensive multidisciplinary approach where pharmacologic treatment is not the sole focus
- Patients experience ongoing barriers to adequate pain management
 - “many related to non-existent or insufficient insurance coverage and reimbursement for evidence- and consensus-based therapies”

-American Academy of Pain Medicine, 2014
- As a result, treatments have largely focused on prescription drugs, mainly opioids, and procedures, at least, in part, because of the reimbursement structure of our healthcare system

FDA Response to this Crisis

"Unquestionably, our greatest immediate challenge is the problem of opioid abuse. This is a public health crisis of staggering human and economic proportion ... we have an important role to play in reducing the rate of new abuse and in giving healthcare providers the tools to reduce exposure to opioids to only clearly appropriate patients, so we can also help reduce the new cases of addiction."

- Scott Gottlieb, FDA Commissioner
Address to FDA staff, May 15, 2017

The Opioid Crisis: An FDA Priority

Take immediate steps to reduce the scope of the epidemic of opioid addiction

- **May 2017:** Established an FDA Opioid Policy Steering Committee (OPSC)
- **2017-2018:** Soliciting public input on how **FDA authorities** can or should be **used to address the crisis**
 - **Sept 2017, January 2018:** Public meetings
 - **December 2017:** Packaging solutions
 - **February 2018:** Healthcare system solutions

The Opioid Crisis: FDA's Priorities

1. Decreasing Exposure & Prevent New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk



FDA Priorities align to HHS Strategic Priorities and other National Activities

HHS STRATEGIC PRIORITIES FDA PRIORITIES OTHER ACTIVITIES

Strengthening public health surveillance

Targeting availability and distribution of overdose-reversing drugs

Supporting cutting-edge research

Improving access to treatment and recovery services

Advancing the practice of pain management

1. Decreasing Exposure & Prevent New Addiction

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President's Commission on Combating Drug Addiction

Office of National Drug Control Policy Recommendations

Comprehensive Addiction and Recovery Act (CARA)

National Pain Strategy Recommendations

National Public Health Emergency

1. Decreasing Exposure and Prevent New Addiction

HOW?

WHAT?



Appropriate Dose/Duration Labeling

- Facilitate appropriate prescribing of opioid analgesics.
- Evaluate **indication specific doses**.

- **Jan 30, 2018:** FDA **public meeting** to gain input on how FDA’s authorities could **facilitate appropriate prescribing**.
- **Feb 15, 2018:** Duke Margolis **public workshop** – “Strategies for Promoting the **Safe Use** and **Appropriate Prescribing** of Prescription Opioids”.



Appropriate Packaging, Storage, and Disposal

- Explore how opioid analgesic drug products are **packaged, stored, and discarded**.
- Examine use of packaging strategies, such as **unit-of-use packaging** to improve opioid analgesic safety.

- **Jun 1, 2017:** FDA/Duke Margolis **workshop and white paper** on packaging, storage, and disposal solutions.
- **Dec 11-12, 2017:** FDA **public workshop** to gain input on **packaging strategies**.

1. Decreasing Exposure and Prevent New Addiction



Health Care Provider Education

HOW?

- Consider appropriateness of **mandatory education** and **how FDA would operationalize** such a requirement.
- Ensure **training** is made **available to non-physician prescribers**, including nurses and pharmacists.

WHAT?

- **May 9-10, 2017:** FDA **public workshop** on pain management training. Issued **revised Blueprint**.
- **Sept 28, 2017:** FDA issued **letters** notifying sponsors of IR opioids their drugs will be subject to more stringent set of requirements under REMS & should be approved Sept 2018. The **training** must be made available to **health care providers** who prescribe **IR opioid analgesics**.

2. Supporting the Treatment of Those With Opioid Use Disorder



HOW?

WHAT?



Naloxone

- Exploring ways to **expand access** to naloxone and **facilitate the switch** to **OTC naloxone**.

- **Precedent setting research: FDA-led labeling study** to facilitate the **switch** from prescription to **OTC naloxone**.



Medication Assisted Treatment (MAT)

- Facilitate the development of **new MAT options**.
- Take steps **promote the more widespread use** of existing, safe and effective, FDA approved therapies.
- Join efforts to **break the stigma** associated with medications used for treatment of addiction.

- Issuing Guidances for product developers to **facilitate the development of new treatments**.
- NIH **collaboration** to identify **new endpoints** in MAT drug development and **facilitate new formulations**.

3. Fostering the Development of Novel Pain Treatment Therapies



Partnerships & Meetings

HOW?

- Expand use of partnerships with **non-profit organizations**, **public meetings**, and **Advisory Committee** meetings.
- **Collaborate** across HHS.

WHAT?

- **FDA grant** supporting Drug-Free Kids campaign.
- **Public-private-partnership (PPP) with NIH and developers** under the Critical Path initiative.
- **Jul 2017:** Commissioned NASEM **consensus report**.
- **Feb 14, 2018: Advisory Committee** meeting for Hydexor (hydrocodone/APAP/promethazine) – for short term **management of acute pain** while **preventing** and **reducing** opioid-induced **nausea** and **vomiting**.

3. Fostering the Development of Novel Pain Treatment Therapies

	HOW?	WHAT?
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Abuse Deterrent Formulations (ADFs)

- Support development of **innovative** ADFs, **data** to inform benefit-risk assessment, and **transition to an ADF-prominent market**.
- Ensure ADF **label nomenclature** enables providers to adequately distinguish between the risk of abuse and the risk of addiction.

- **Jul 2017: Public workshop** for postmarketing **ADF data and evaluation methods**.
- Issued final **guidance** on **generic ADFs**.
- **2018: Contracts** to improve **data for ADF assessment** and understand **nomenclature**.





Pain Treatment Alternatives

- Explore use of Fast Track and Breakthrough Therapy Designations.
- Encourage novel therapies, including **medical devices**.

- **Summer 2017: FDA/NIH meeting series** on pain treatment alternatives.

4. Improving Enforcement & Assessing Benefit-Risk

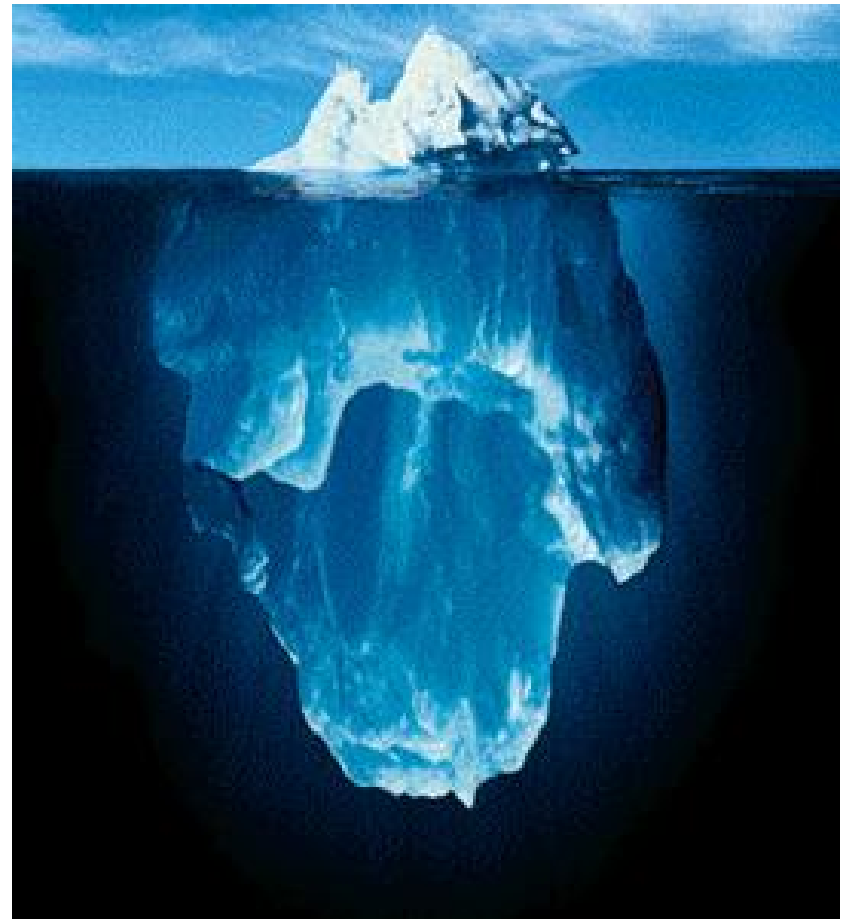
	HOW?	WHAT?
 <p>Improving Enforcement</p>	<ul style="list-style-type: none"> Consider how to fully leverage FDA's current seizure authorities. Increase oversight of illicit trade. 	<ul style="list-style-type: none"> Collaboration with Customs and Border Protection to increase FDA staff stationed at international mail facilities (IMFs) to increase seizure of opioids being smuggled into the United States through international mail facilities (IMFs).
<hr/>  <p>Assessing Benefit-Risk</p>	<ul style="list-style-type: none"> Take action, including product market withdrawal recommendation. Improve robustness of benefit-risk assessment framework for opioid analgesic formulations. 	<ul style="list-style-type: none"> Jun 2017: Requested market withdrawal of Opana ER due to abuse risks. Sep 2017: Pediatric Advisory Committee for hydrocodone or codeine containing cough treatment in pediatric patients.

FDA Will Use All of its Available Tools to Accomplish These Goals

- Improving the safe use of opioids through careful and appropriate **regulatory activities**
- Improving the safe use of opioids through careful and appropriate **policy development**
- Improving the treatment of pain through **improved science**
- Improving the safe use of opioids through **communication, partnership and collaboration**

Solutions Must Come from Many Sources

- FDA is one of many Federal agencies addressing issues involving opioids
- Many Federal Agencies working together on issue
- Each state has programs to address opioids
- Guidelines and educational programs are available from specialty societies and State Medical Boards
- Healthcare institutions
- Advocacy groups
- Individual providers (n = 800,000+)
- Patients (n = millions)



Summary and Conclusions

- FDA working to address opioid epidemic as a part of the larger HHS response
 - One of the FDA’s very highest priorities
 - FDA one of many groups focused on the issue
- Going forward, FDA is committed to taking decisive actions, grounded in the available science and appropriate public input to address this critical challenge to the US health and welfare
- Our focus is addressing opioid abuse while assuring appropriate access to effective pain treatment

Thank You

