

Ongoing FDA Work Related to Opioid Overdose Prevention

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Recent and Ongoing Activities Related to Naloxone



- Co-prescribing of Naloxone with RX Opioids
 - Results of recent public FDA Advisory Committee
- Over-the-Counter (OTC) Naloxone
 - Research to support labeling for OTC naloxone products to support product development
- Role of expanded naloxone availability in USG response to opioid crisis
 - Systems model of opioid crisis

The Opioid Crisis: FDA's Priorities & Strategies



1. Decreasing Exposure & Prevent New Addiction





Health Care Provider Education

2. Supporting the Treatment of Those With Opioid Use Disorder



Medication Assisted Treatment (MAT)

3. Fostering the Development of Novel Pain Treatment Therapies

- Partnerships & Meetings
 - Abuse Deterrent Formulations (ADFs)
 - ✓ Pain Treatment Alternatives

4. Improving Enforcement & Assessing Benefit-Risk

- Improving Enforcement
- Assessing Benefit-Risk

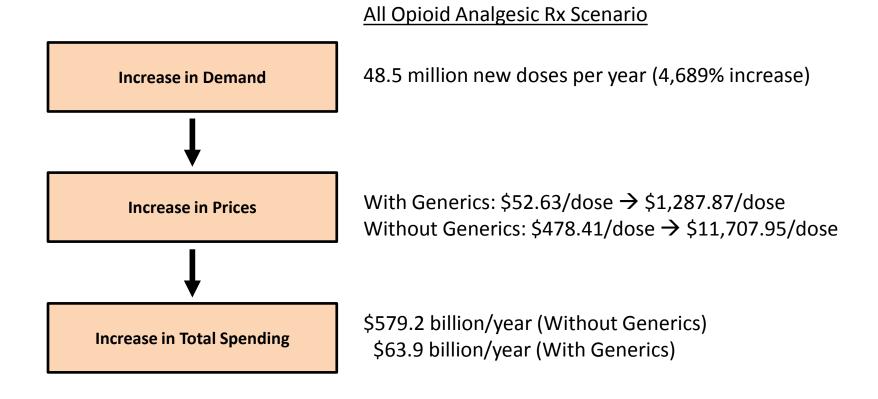
I. Naloxone Co-Prescribing with Rx Opioids



- Naloxone prescriptions rising (336.1K dispensed in 2017) but still inadequate
- FDA received Citizen Petition from maker of one of the naloxone products requesting FDA require coprescribing of patients prescribed opioids
- FDA Advisory Committee held December 17-18 to get input from advisors and public

Annual Cost of Requiring Co-Prescribing: FDA Model





Naloxone Advisory Committee (cont)



- In general:
 - Harm reduction advocacy groups very strong in their view that co-prescribing was not 'enough'
 - Committee members not supportive of value of required coprescribing
 - Concerns expressed about cost to healthcare system and diversion of resources (both money and naloxone) away from underserved areas
 - Focus should be on educating prescribers/patients and supporting harm reduction efforts
- In addition, Committee members called on USG to take on broader actions to 'force' expanded availability of naloxone. Examples:
 - Forced OTC switch
 - Revoking patents currently delaying generic/OTC product marketing
 - Manufacturing naloxone and making it available from USG stockpile(s)
 - Extending expiration dating for naloxone products

Next Steps



- FDA meeting internally on AC recommendations
 - Plan response to Citizen Petition
 - Discuss ideas raised by Committee membersReview
 AC Docket comments (>220 comments received so far)
 - Engage external stakeholders
 - Propose next steps to leadership

II. Over-The-Counter Naloxone: Why OTC Naloxone?



- Existing expanded access programs (such as pharmacy standing order programs) are a significant tool, but more is needed – not everyone can/wants to obtain the product through a healthcare professional
- Surgeon General's 2018 Advisory

U.S. Surgeon General Advisory



"I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life."

Development Programs for Nonprescription Drugs



- Often rely on safety and efficacy established for the prescription product
- New studies may be required if proposing a new indication or a new patient population for the OTC market
- Need to "translate" key elements of the prescription label into consumer-friendly terms
- Consumer studies needed to evaluate the "OTC-ness" of product

Translate the Approved RX Product Label....



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To a Label for OTC Products.....



Drug Facts Label

Drug Facts		
Active ingredient (in each tablet) Chlorpheniramine maleate 2 mgAntii		
Uses temporarily relieves these symptoms allergies: ■ sneezing ■ runny nose ■ it		
Warnings Ask a doctor before use if you have ■ glaucoma ■ a breathing problem such as ■ trouble urinating due to an enlarged prostat	e gland	
Ask a doctor or pharmacist before use if y	ou are taking tranquilizers or sedatives	
When using this product ■ drowsiness may occur ■ avoid alcoholic ■ alcohol, sedatives, and tranquilizers may in ■ be careful when driving a motor vehicle or of ■ excitability may occur, especially in children	crease drowsiness operating machinery	
If pregnant or breast-feeding, ask a health present of reach of children. In case of or Control Center right away.	professional before use. verdose, get medical help or contact a Poison	
Directions adults and children 12 years and over	take 2 tablets every 4 to 6 hours; not more than 12 tablets in 24 hours	
children 6 years to under 12 years	take 1 tablet every 4 to 6 hours; not more than 6 tablets in 24 hours	
children under 6 years	ask a doctor	

Drug Facts (continued)	
Other information ■ store at 20-25° C (68-77° F)	■ protect from excessive moisture
Inactive ingredients D&C yellow no. 10, lactose, recellulose, pregelatinized starch	magnesium stearate, microcrystalline

OTC Consumer Studies



Label Comprehension Study

Understanding the key label messages

Self-Selection Study

• Choosing the right product for "me"

Actual Use Study

Using according to labeled directions

Human Factors Study

Interacting with the product



FDA Proposed an Innovative Approach to Support OTC Naloxone Products:

- To develop a model Drug Facts Label (DFL) that could be understood by all potential consumers who might use OTC naloxone
- To iteratively refine the DFL and evaluate consumer comprehension through a contract with established consumer research firms with expertise in conducting label comprehension studies and interviewing substance abuse populations
- To conduct an independent review of the resulting data



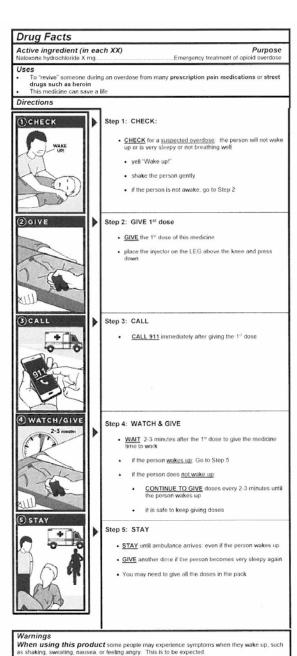


- If study was successful, Sponsors could adapt the model DFL to their naloxone product
- Sponsors would only need to add information specific to their particular device and assess through human factors
- Label comprehension was the key study to be conducted – self-selection and actual use are likely not needed

Status of Research



- FDA-supported study completed December 2018
- Review by FDA scientists complete January 2019
 - FDA concluded that the results of this study are acceptable to support use of the tested naloxone DFL in the OTC setting
 - FDA in the process of making these results and findings public for use by manufacturers seeking to develop OTC naloxone products
 - FRN in clearance
 - Planned public announcement of results and article being written



Other information • store at room temperature • [advise insert tamper evident statement here]

Inactive Ingredients

Questions?
(phone number, website)

Prototype Drug Facts Box for OTC Naloxone

III. Systems Model of Opioids Crisis Including Role of Naloxone



- Deliverable for the BHCC
- Successful model will help identify high-impact actions and anticipate consequences of policy changes
- Experts from across HHS providing input



OVERVIEW: WHY MODELING

Events

Every day, more than 115 people in the United States die after overdosing on opioids...



The total number of overdose death has been on the rise.



System architecture

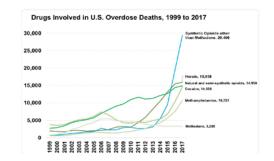
- · Feedback processes
- · Stocks and flows
- · Time delays

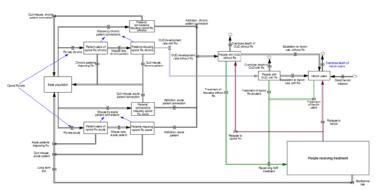
Information availability

- Delays, biases, error, gaps
- Access & transparency

Mental models (of any stakeholder)

- · Actor goals and incentives
- Time horizon, model boundary
- Misperceptions of feedback

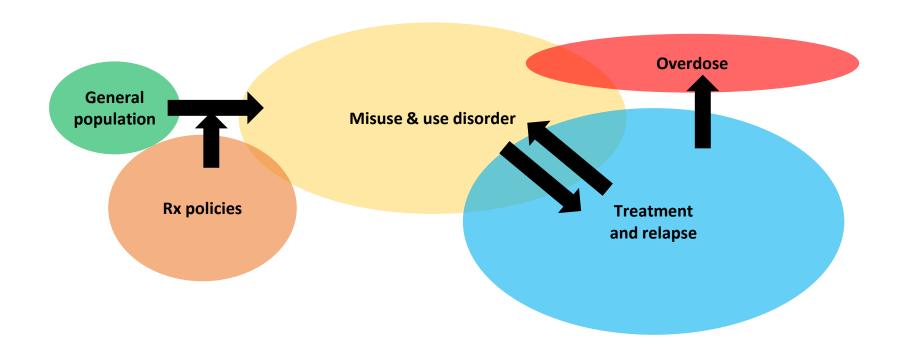




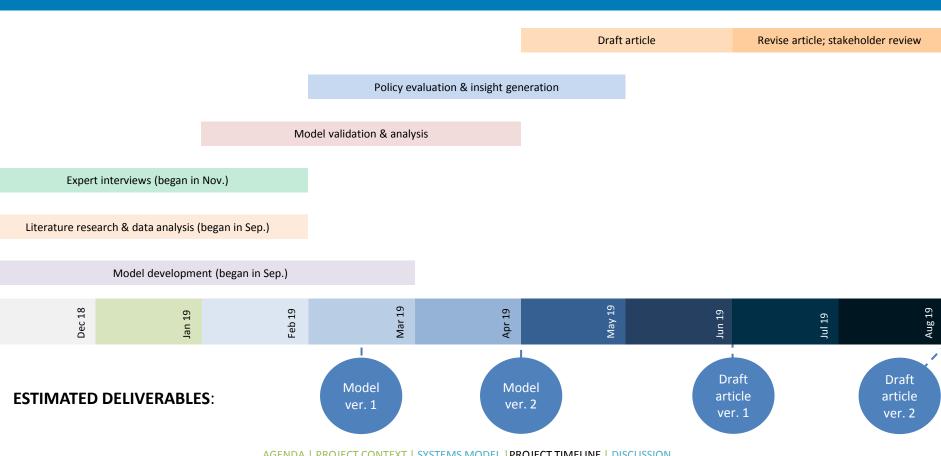
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Elements of Opioid Use/Misuse/Abuse Model (Simplified)



PROJECT TIMELINE





Thank You





Backup Slides



FDA Estimates Differ from the Manufacturers Based on Several Key Assumptions

Key Assumption	FDA Model	Industry Model
Targeted Patient Population(s)	0.3-58.0 million	34.0 million
Compliance Rate	100% Prescribing; 70% Fill	8-10% Dispensed
Price Increase	Yes (up to 2,347%)	No
Prescription Fill Costs	Yes (\$3.94/dose)	No

FDA Estimate for Industry Population With 70% Adoption:

\$24.7 Billion/Year - \$224.0 Billion/Year

FDA Estimate for Industry Population With 8% Adoption:

\$0.5 Billion/Year - \$4.7 Billion/Year (Industry: \$150 Million/Year)



Total Annual Costs— Naloxone Co-prescribing for All Opioid Analgesic Rx Estimated At \$63.9 Billion - \$579.2 Billion

New Doses (With Generics):

48.5 Million x ($$1,287.87 + $3.94^{1,2}$) = \$62.6 billion

Existing Doses (With Generics):

1.0 Million x (\$1,287.87 - \$52.63) = \$1.3 billion

Total (With Generics): = \$63.9 billion

¹Coalition for Community Pharmacy Action. The Cost of Dispensing Study. September 2015.

²Takes the payroll and prescription department costs per prescription and divides this number by 2 to convert it to a per-dose basis



Results: Patient Groups That Interact With the Health System

Population	# Patients (Millions)	Annual Cost w/ Generics (\$ Billions)	Annual Cost w/o Generics (\$ Billions)
All Opioid Analgesic Rx	58.0	63.9	579.2
High-Impact Chronic Pain	19.6	9.5	85.5
Rx Opioid Analgesics with CNS	3.5	0.6	5.3
Depressants			
Medication Assisted Treatment (MAT)	1.4	0.2	1.5
Opioid-Related ED Visit	0.8	0.1	0.7



Results: Patient Groups That Don't Interact With the Health System

Population		Annual Cost w/ Generics (\$ Billions)	Annual Cost w/o Generics (\$ Billions)
Misusing Opioids	11.4	3.8	34.0
Opioid Use Disorder	2.1	0.3	2.5
Recent Criminal Justice and Rx Opioid Misuse	0.9	0.1	0.8
Recent Criminal Justice and Heroin Use	0.4	< 0.1	0.3
Recent Criminal Justice and Opioid Use	0.3	< 0.1	0.2
Disorder			



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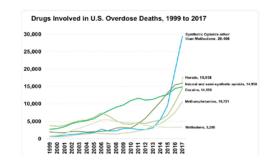
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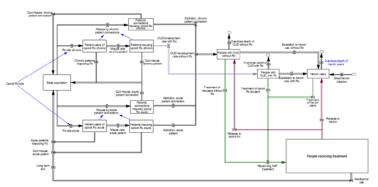
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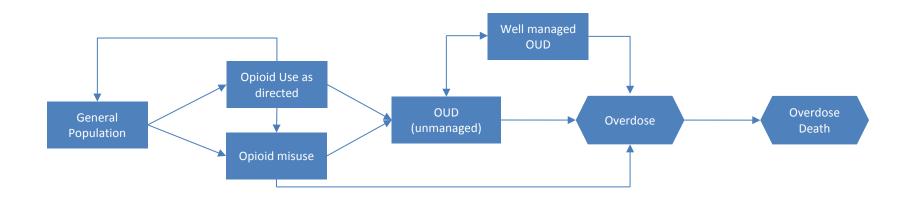




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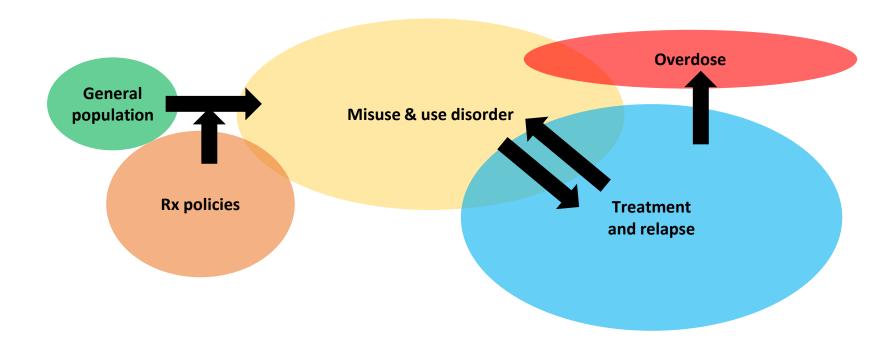


MODEL BACKBONE





Illustrative pathway (simplified)





Illustrative pathway (detailed)

