Research Funding Opportunities to Reduce Preventable Harm

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1/28/2020

Disclaimer

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Objectives

- Explain the criteria for applying for funding through the Safe Use Initiative
- Outline the stages of the Broad Agency Announcement (BAA) evaluation process
- Describe qualities that make for a strong research project

Safe Use: Mission and Goal

Mission: to create and facilitate public and private collaborations within the healthcare community.

Goal: to *reduce preventable harm* by identifying specific, preventable medication risks and developing, implementing and evaluating cross-sector interventions with partners who are committed to safe medication use.

https://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/default.htm

Funding Extramural Research

- One method used by Safe Use to fulfill its mission and goal is by funding extramural research.
- Projects are funded through the Broad Agency Announcement or BAA.
- Details can be found on the Safe Use Extramural Research page : https://www.fda.gov/drugs/safe-use-initiative/safe-use-initiative-extramural-research or at beta.SAM.gov

BAA Funding Mechanism

“FDA Broad Agency Announcement for the Advanced Research and Development of Regulatory Science”

“The U.S. Food and Drug Administration has an **open, continuing announcement** to **solicit research** and development **in support of regulatory science and innovation**. The Safe Use Initiative welcomes proposals to this announcement which support its mission and goal.”

https://www.fda.gov/drugs/safe-use-initiative/safe-use-initiative-extramural-research

Unique Aspects of the BAA Mechanism

- Safe Use welcomes the opportunity to have a conversation about research ideas and project concepts.
  - All discussions must take place **before** submission of the White Paper.
- Projects funded via the BAA result in a contract, not a grant.
- If funded, researchers must provide a brief written update monthly and a final report at project completion.

Research Priority Areas

The FDA has defined several “research priority areas.”

- Safe Use falls under **Area 8**: “Strengthen Social and Behavioral Science to Promote Informed Decision-Making About FDA-Regulated Products.”
- Specifically, Safe Use is **Area 8.5.1**: “Studies that develop innovative methods to create, facilitate and encourage research in the area of safe medication use that seeks to *reduce preventable harm from drugs.*”

https://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm277720.htm

Safe Use Partners

- Healthcare professionals and professional societies
- Pharmacies, hospitals, and other health care entities
- Patients, caregivers, consumers, and their representative organizations

= Almost anyone

Current Safe Use Projects

- Safe Use has 8 current projects.
- Safe Use has funded 26 projects involving a wide variety of drugs and potential adverse events.
  - Opioids
  - Anticoagulants
  - Antibiotics
  - Anti-hyperglycemic agents
  - Stimulants
  - Pediatric cough and cold medications
  - NSAIDS

https://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm277720.htm

How do you Reduce Preventable Harm?

- Identify patients at highest risk
- Use of technology
- Provider and facility feedback and/or self-assessment
- Make medications easier to use
- Improve communication

➢ **There is no “one size fits all” solution**

Desirable Qualities

1. The subject must be related to or impact an FDA/ CDER-regulated product.
   - Project can relate to a class of drugs (antibiotics) or can be more broad in scope (safe storage and disposal).

2. Project must aim to reduce a preventable harm.
   - Proposal should clearly describe the harm to be reduced and how the project intends to accomplish this goal.

Desirable Qualities

3. Impactful
   - Harms to be reduced should be clinically meaningful and address an unmet public health need.
   - Target population can be broad (addresses a common high-burden disease) or narrow (a vulnerable population such as very young, veterans, or stigmatized populations).
4. Measurable Outcome
   - The strongest projects are built around a measurable outcome to assess intervention effectiveness.
     - Measure can be direct (hospitalizations) or indirect (reduced number of prescriptions).

Desirable Qualities

5. Results should be actionable and/or scalable
   - Most projects are conducted at one or a few sites.
   - Safe Use favors projects that have the potential to be easily and widely adopted.

6. Innovative methods
   - Projects that use innovative methods or combine methods in novel ways are encouraged.

How to Apply

- Applying for funding via the BAA is a 2 stage process.
  - Stage 1: Quad Chart and White Paper
  - Stage 2: Full Proposal (if invited)

Proposal Stage	Deadline for Submission
Stage 1: Quad Chart and White Paper	**Anytime during open period**
Stage 2: Full Proposal	**Within 30 calendar days of Invitation (unless designated otherwise by the CO)**

Stage 1: Quad Chart

TITLE OF PROJECT, MOST APPLICABLE RESEARCH AREA ADDRESSED
PROGRAM DIRECTOR/MANAGER, COMPANY NAME

Objective: Clear, concise (2-3 sentences) description of the objectives and methodologies of the effort. Description of Effort: A bullet list (2-3) of the primary scientific challenges being addressed	Picture or Graphic that illustrates the research or concept (e.g. data figures, molecule illustrations of processes)
Benefits of Proposed Technology: Challenges: Research and Development Justification:	Bullet list of the major goals/milestones by Project Year Proposed Funding: Base period cost plus each option period (no more than 5 years total) **Contact Information (name, email, phone)**

Stage 1: White Paper

- Expands upon the information in the Quad Chart
- **Maximum** of 10 pages
- The White Paper needs to explain the project's objectives, why the project is important, and how the objectives will be accomplished.
- Please provide enough technical details to allow a reviewer to evaluate the project's technical merit and its potential contribution to the FDA mission.

Stage 1: White Paper

- Safe Use forms a committee of subject matter experts who review and evaluate the White Paper.
  - Reviewers rate the project independently, then meet to reach a consensus.
- Decision is to invite or not invite a full proposal.
- Reviewers evaluate three areas (in decreasing order of importance):
  - Scientific and Technical Merit
  - Program Relevance
  - Capabilities and Experience

Scientific and Technical Merit

- Soundness, feasibility, and validity of the proposed project, including reasonableness of the proposed schedule and understanding of any relevant statutory and regulatory requirements
- Degree of innovation and potential to increase capability or decrease costs
- Understanding of the scope and technical effort needed

Program Relevance

- Does the project address an important problem or critical barrier?
- If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved?
- How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventive interventions in this field?

Capabilities and Experience

- Qualifications, capabilities, and experience of the principal investigator and research team
- Offeror's demonstrated ability for achieving the proposal objectives
- Research Management: Overall capability to manage the effort, including plans to measure the value and impact of the research

Stage 2: Full Proposal

- A Full Proposal consists of 2 volumes.
- Volume 1 is the Technical Proposal.
  - Expands on the White Paper
  - Provides additional details on methods to be used and analyses to be conducted
  - **Maximum** of 50 pages
- Volume 2 is the cost proposal.
  - Should contain sufficient detail for meaningful cost evaluation
  - Limited to 20 pages

Stage 2: Full Proposal Evaluation

- Committee is formed and proposal is rated
- Criteria for evaluation are the same as the White Paper stage:
  - Scientific and Technical Merit
  - Program Relevance
  - Capabilities and Experience
- Awards are made based on proposal evaluation, funding availability, and other programmatic considerations.

FY2020 Funding Cycle

- We are currently accepting proposals for FY2020 funding.
- White Papers must be received by **March 2, 2020**.
  - Proposals received after the deadline will be considered for FY2021 funding.
- Any proposal selected for funding must result in a signed contract by September 30, 2020.

Examples of Safe Use Funded Projects

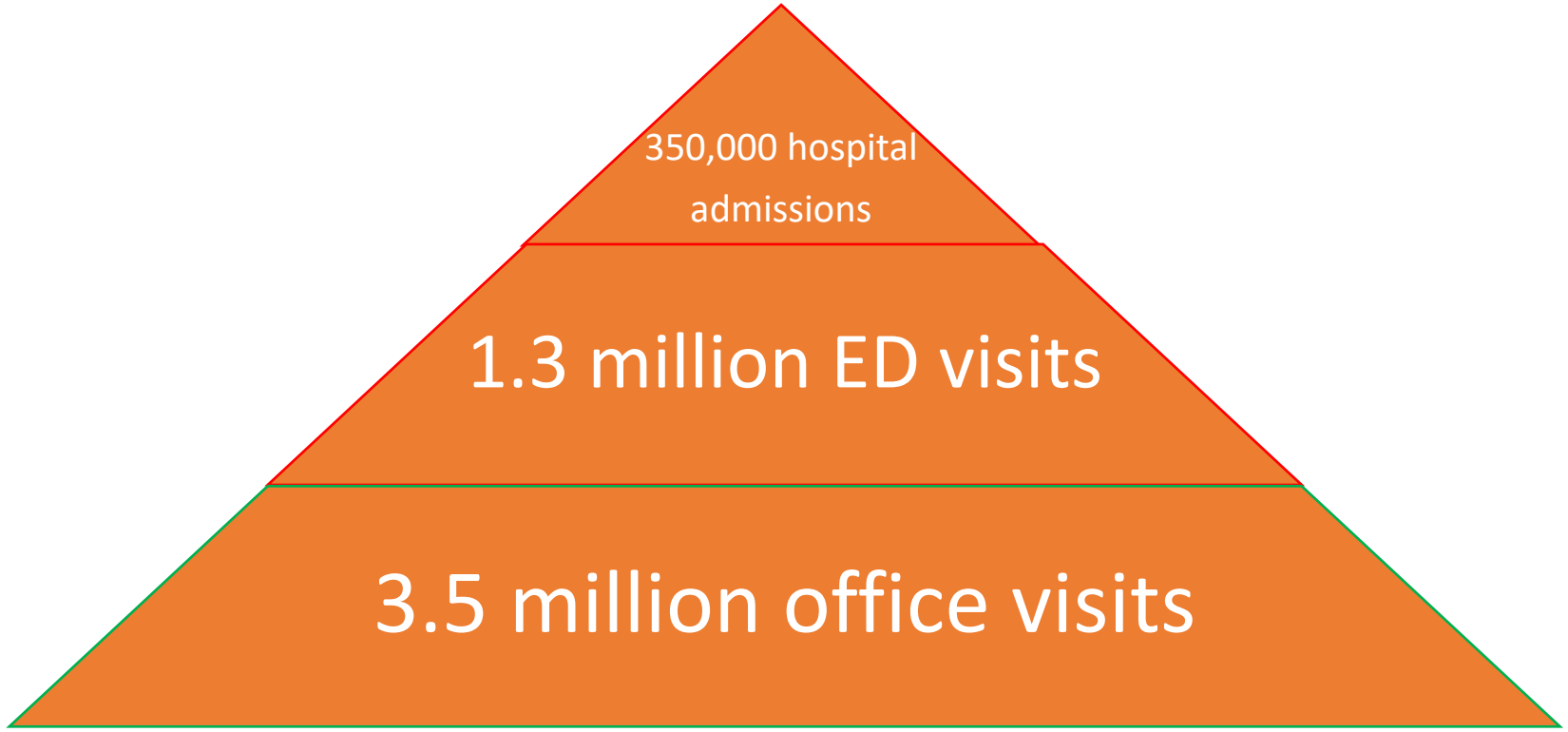
- Core Elements of Anticoagulation Stewardship
- Improving Safe Use of Fluoroquinolone Antibiotics Through Development of an Innovative Education Program
- A Scalable, Patient-Centered Approach for “Right-sizing” Opioid Prescribing

Example 1: Core Elements of Anticoagulation Stewardship

Objectives

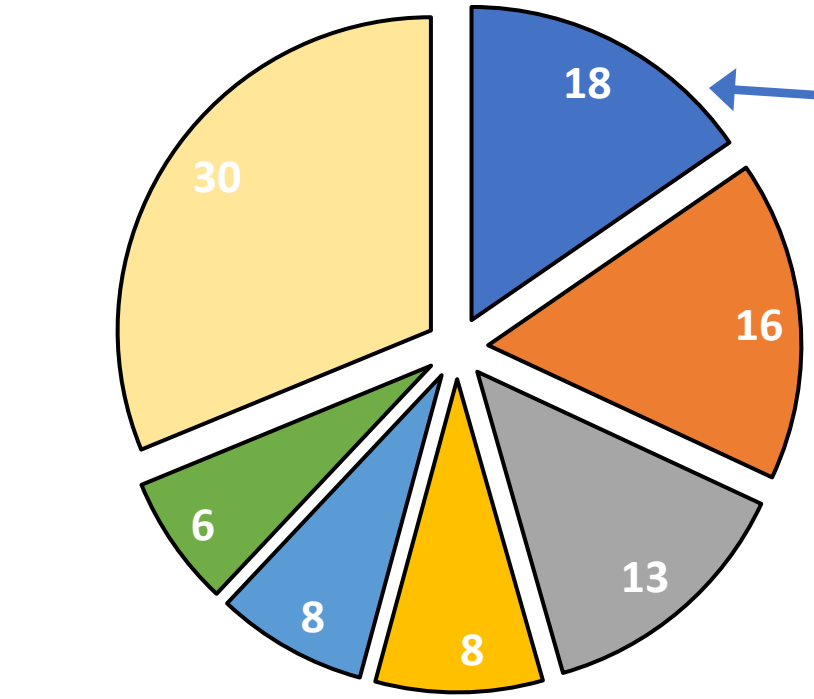
- Increase awareness of deficiencies in the quality and safety of anticoagulation management
- Produce and disseminate three high-priority deliverables
  - A Core Elements of Anticoagulation Stewardship Guide
  - A Self-Assessment Tool
  - An Administrative Oversight Gap Report

Outpatient Adverse Drug Event Results 2013-2014*



*Shehab N, et al. US emergency department visits for outpatient adverse drug events 2013-2014. 2016 Nov;316(20):2115-2125

ED Visits for ADEs by Medication Class



18% of ED visits for ADEs from **Anticoagulants**
-15% from warfarin
-3% from other anticoagulants

Anticoagulants
Antibiotics
Diabetic agents
Analgesics
Cardiovascular Agents
Antiplatelet
Other Classes

*Shehab N, et al. US emergency department visits for outpatient adverse drug events 2013-2014. 2016 Nov;316(20):2115-2125.

Core Elements of Anticoagulation Stewardship

- Project has been completed and Guides are available at the Safe Use website:

https://www.fda.gov/drugs/safe-use-initiative/safe-use-initiative-extramural-research

or from the Anticoagulation Forum site:
https://acforum.org/web/education-stewardship.php

Core Elements of Anticoagulation Stewardship

Desirable Qualities

- Subject is a class of CDER-regulated products.
- Project addresses harms such as bleeding, improper dosing, inappropriate prescribing.
- Harms to be addressed are clinically meaningful and impact a large population.
- Implementation is scalable and has potential to be widely adopted.

Example 2: Improving Safe Use of Fluoroquinolone Antibiotics

Objective

- Evaluate effect of targeted short-form messages (TSFMs) on fluoroquinolone prescribing among high prescribers.

Method

- Three phases (using Medscape):
  1. Match prescribers and their individual fluoroquinolone prescribing data with controls*
  2. Provide feedback to prescribers
  3. Assess changes in prescribing patterns

*matched on profession, specialty, geography, and pre-test period prescribing

Safe Use of Fluoroquinolone Antibiotics

- Antimicrobial Drugs Advisory Committee and the Drug Risk and Safety Management Advisory Committee – Nov 15, 2015 voted:

  Benefits and risks of systemic fluoroquinolone antibacterial drugs DO NOT support current labeled indications for treatment of:

  - Acute bacterial sinusitis
  - Acute bacterial exacerbation of chronic bronchitis in patients with COPD
  - Uncomplicated UTI

Identifying and Targeting Frequent Fluoroquinolone Prescribers

- Data available for 320,479 prescribers over a 1 year period
- Approximately 14.5 million fluoroquinolone prescriptions written
- Of these, ~50% were written by 8.7% of prescribers (28,000 “high-tier prescribers”)

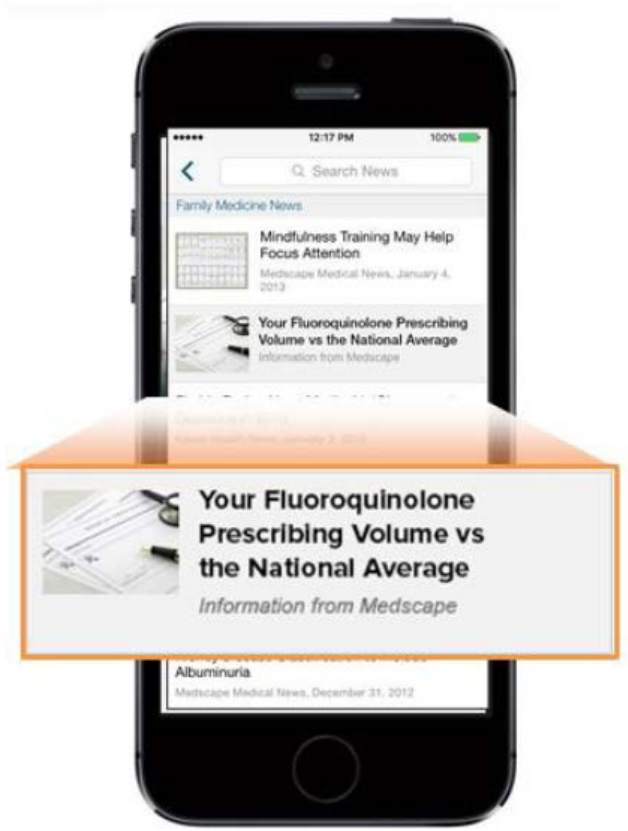
Provide Feedback to Prescribers

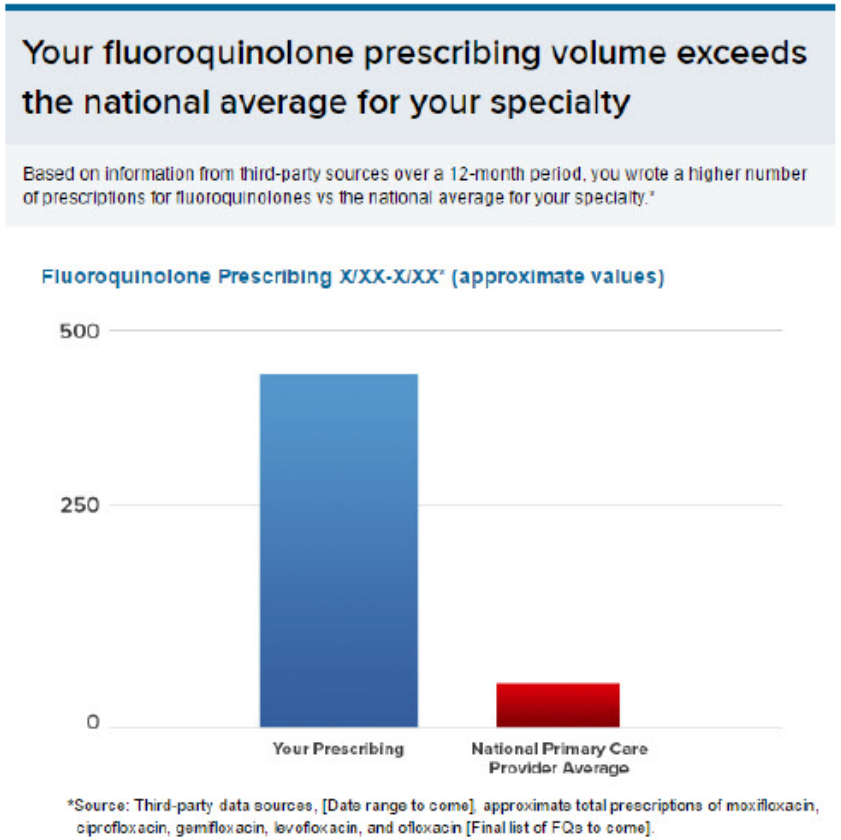
- High-tier prescribers received email and messages when they logged onto Medscape
- Messages differed for each of 3 groups:

Segment	Prescribers (n)	Message	Individual Prescribing Level*	Clinical Context and Resources
1	9,333	A	✓	
2	9,333	B	✓	✓
3	9,333	C		✓

*In context of national average for specialty

Examples of Individualized Feedback





Outcome Measures

Does fluoroquinolone prescribing decrease?

- Overall impact – comparing prescribers who engaged in the intervention to controls
- By sub-groups (urologists, primary care MDs, all other MDs, NPs and PAs)
- By intervention group (individual data only, clinical context only, both)
- By specified indication

Information Received and Changes in Prescribing

	Test vs. Control Differences
Targeted Short Form Messages	**NRx Volume (p-value)**
Message A*: Personalized prescribing level in context of national average in specialty (n=3,057)	-7.9% (p<0.0001)
Message B*: Personalized prescribing level/context AND Clinical Content (n=3,009)	-9.4% (p<0.0001)
Message C*: Clinical content & resources describing risks associated with fluoroquinolones (n=2,822)	-8.2% (p<0.0001)

*There are no significant differences in level of impact resulting from exposure to Message A, B, or C

- Intervention significantly reduced prescribing relative to control for all groups

Reduced Prescribing by Specialty

HCP Category	NRx Volume Compared with Control (p-value)
Primary Care MDs (n=6201)	-10.1% (*P*<0.0001)
Urologist MDs (n=1099)	-10.8% (*P*<0.0001)
All Other MDs (n=2717)	-11.8% (*P*<0.0001)
NPs/PAs (n=1757)	-7.6% (*P*<0.0011)

- Intervention significantly reduced prescribing relative to control for all groups

Reduced Fluoroquinolone Prescribing by Indication

Diagnosis	NRx Volume Compared with Control
Acute Bacterial Sinusitis (Test n=7819; Control n=7793)	-12.8% (*P*=0.0015)
COPD (Test n=6188; Control n=6040)	-4.5% (*P*=0.2061)
Uncomplicated Urinary Tract Infection (Test n=9446; Control n=9313)	-9.0% (*P*<0.0001)

- Prescribing volume reduced 12.8% for acute sinusitis and 9.0% for uncomplicated UTI
- Non-statistically significant 4.5% reduction in prescriptions for COPD patients

Improving Safe Use of Fluoroquinolones

Desirable Qualities

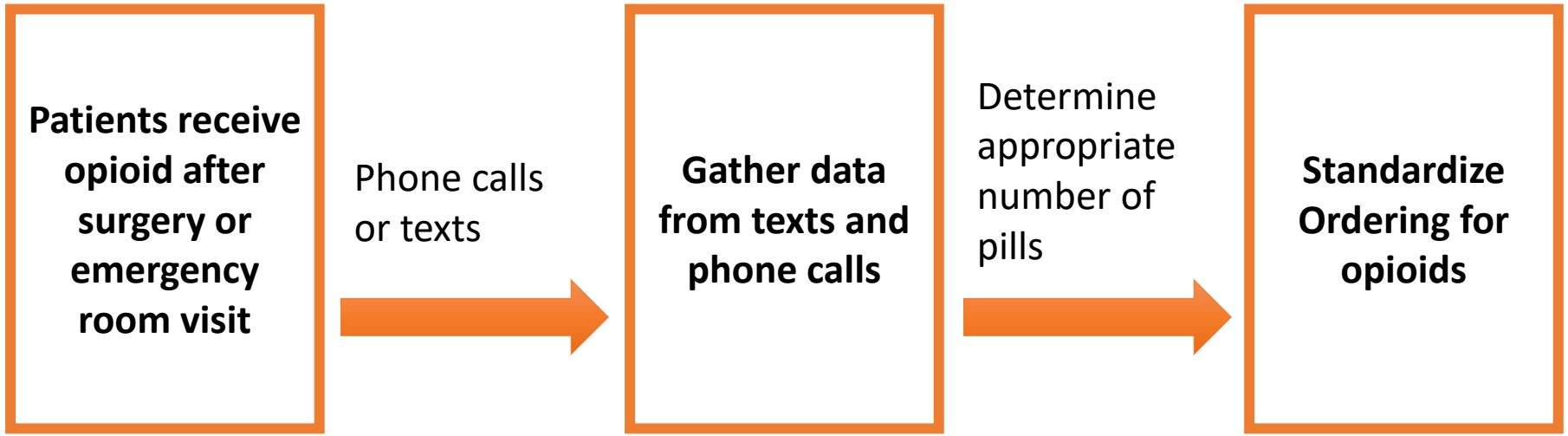
- Subject is a class of CDER-regulated products.
- Project addresses harm related to over-prescribing of antibiotics.
- Harms to be addressed are clinically meaningful and impact a large population.
- Measurable outcome: reduction in prescribing compared to a control population.
- Innovative method: combined individual level prescribing data with messaging via Medscape

Example 3: A Scalable, Patient-Centered Approach for "Right-sizing" Opioid Prescribing

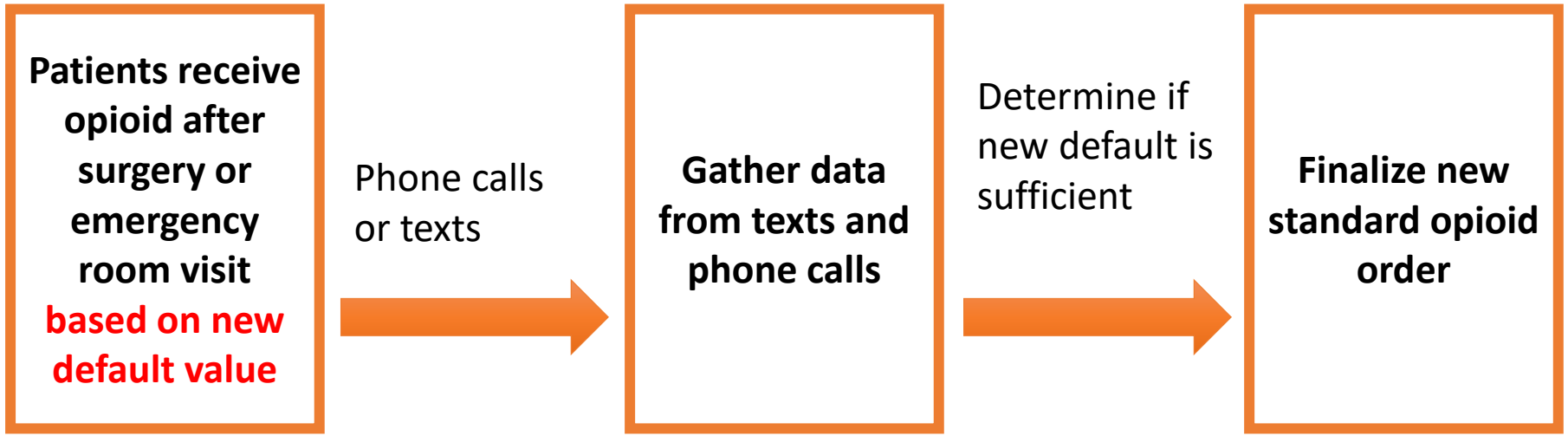
Objectives

- Generate evidence-based and patient-centered acute opioid prescribing guidelines
  - 12 indications (Orthopedics, Neurosurgery, Emergency Department)
- Decrease excessive opioid prescribing
- Avoid unintended consequences that result in patient harm

Scalable, Patient-Centered Approach for Right-Sizing Opioid Prescribing



Scalable, Patient-Centered Approach for Right-Sizing Opioid Prescribing



Scalable, Patient-Centered Approach for Right-Sizing Opioid Prescribing

Observations based on early data

- There is substantial opportunity to reduce the quantity prescribed and still provide pain control.
- In many indications, there are patients who used no opioids and patients who used the full supply.
  - Pain is a highly individualized experience.

Scalable, Patient-Centered Approach for Right-Sizing Opioid Prescribing

Desirable Qualities

- Subject is a class of CDER-regulated products.
- Project addresses harm related to over-prescribing of opioids.
- Harms to be addressed are clinically meaningful and impact a large population.
- Measurable outcome: reduction in prescribing while ensuring patients have access to medication for pain control.
- Scalable: default prescriptions could be adopted by other institutions or method could be applied to other indications.
- Innovative method: uses patient reported data to assess actual use of pain medication after surgery.

Summary

- Funding is available to support research aimed at reducing drug-related preventable harm.
- Stage1: Submit a 10-page White Paper.
- Deadline to submit White Paper for FY2020: **March 2, 2020**.
- FDA will gladly discuss ideas **before** White Paper submission.
- Contact us at CDERSafeUseInitiative@fda.hhs.gov

References

- Core Elements of Anticoagulation Stewardship Programs. Available for download at: https://acforum.org/web/education-stewardship.php

- Delgado MK, Shofer FS, Patel MS, et al. Association between Electronic Medical Record Implementation of Default Opioid Prescription Quantities and Prescribing Behavior in Two Emergency Departments. J Gen Intern Med. 2018 Apr;33(4):409-411.

References

- FDA Broad Agency Announcement (BAA)
- Safe Use Initiative – Extramural Research page