

AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

AHRQ

June 2021 CDS Connect Work Group Call

CDS Connect

Meeting Agenda

Schedule	Topic
3:00 - 3:02	• Roll Call, Michelle Lenox (MITRE)
3:02 - 3:05	• Review of the Agenda, Maria Michaels (CDC)
3:05 - 3:50	• Using CDS to Reduce Harm From Drug-Drug Interactions: Case Study of Warfarin and Non-Steroidal Anti-inflammatory Drugs (University of Pittsburgh; University of Utah)
3:50 - 3:55	• What's New with CDS Connect This Month (MITRE)
3:55 - 4:00	Open Discussion and Close Out, Maria Michaels (CDC) • Open discussion and announcements • Concluding comments, review next steps and adjourn

Objectives

- Share lessons learned on development of CDS
- Share new features and resources available for CDS Connect
- Discuss topics of interest to members relating to opportunities for CDS Connect, including launch of patient partnering panel

SHARING LESSONS LEARNED WITH CDS - Using CDS to Reduce Harm From Drug-Drug Interactions: Case Study of Warfarin and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Richard Boyce, University of Pittsburgh
Dan Malone, University of Utah

Disclosures

Rich Boyce: Neither myself or my spouse have any relevant financial relationships with commercial interests

Dan Malone: Neither myself or my spouse have any relevant financial relationships with commercial interests

Outline

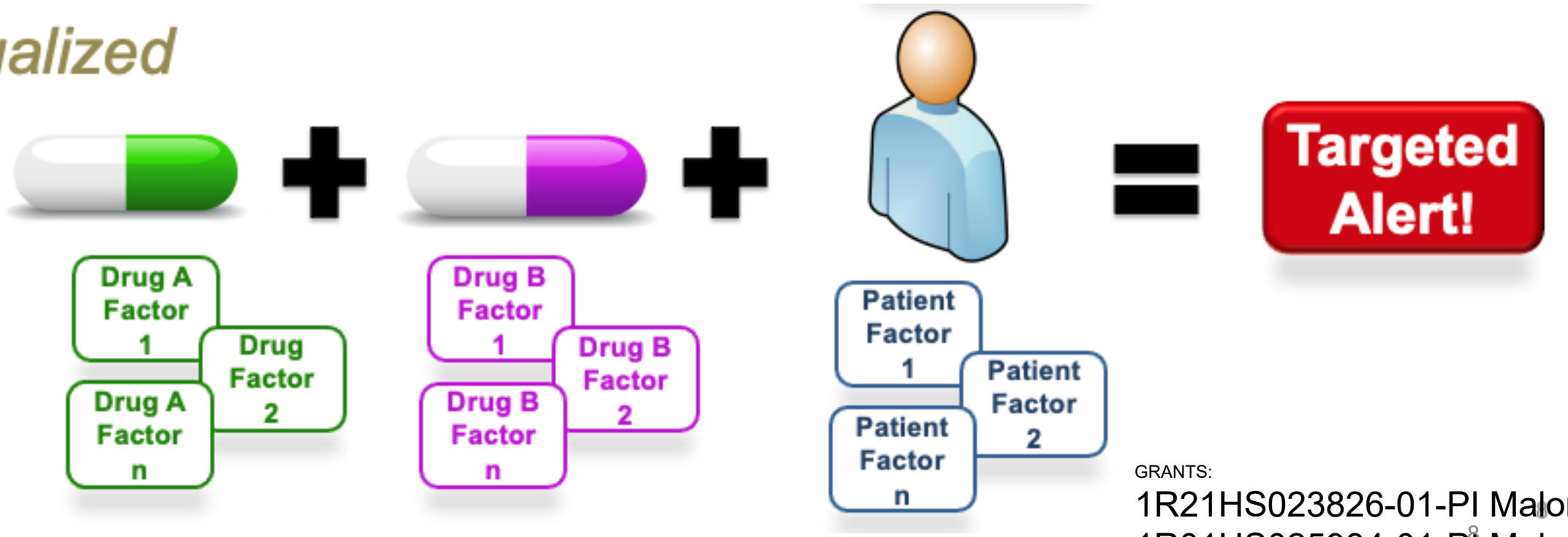
- The use case:
  Contextualized drug-drug interaction clinical decision support
- Authoring structured potential drug-drug interaction CDS
- Shared decision making via DDInteract™
- Discussion

The Use Case: Contextualized Drug-Drug Interaction Clinical Decision Support

The Use Case:
Contextualized drug-drug interaction CDS

Conventional Alerts:

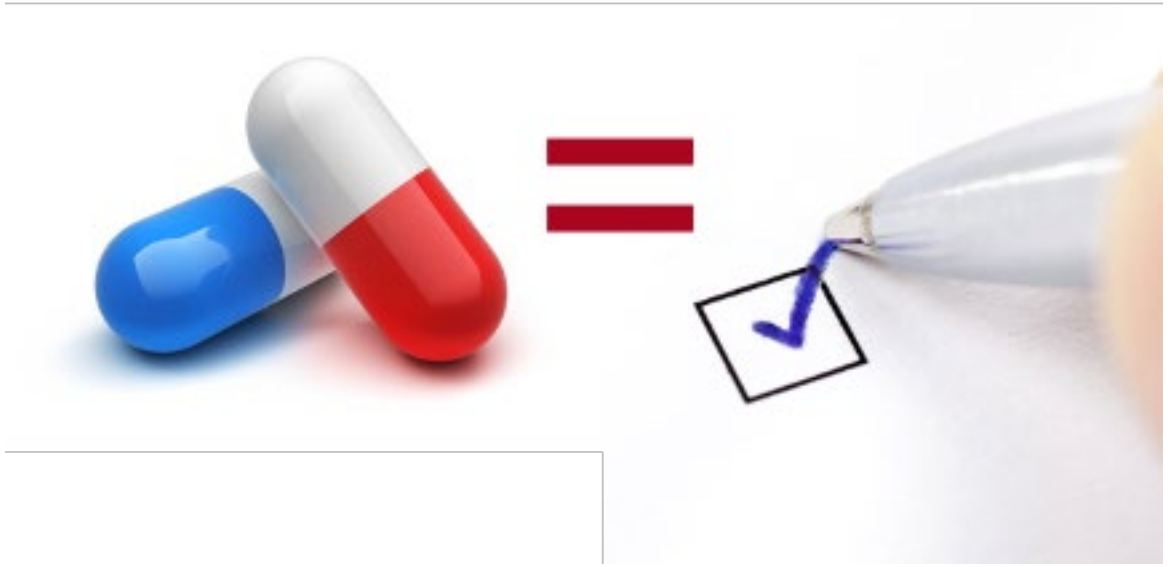
Individualized Alerts:



GRANTS:
1R21HS023826-01-PI Malone
1R01HS025984-01-PI Malone

Potential drug-drug interactions (PDDIs)

- Exposure to two or more drugs that are known to interact
  - "Potential" because exposure does not necessarily mean a clinically meaningful effect
    - Co-prescription or co-administration of drugs known to interact, regardless of whether harm ensues



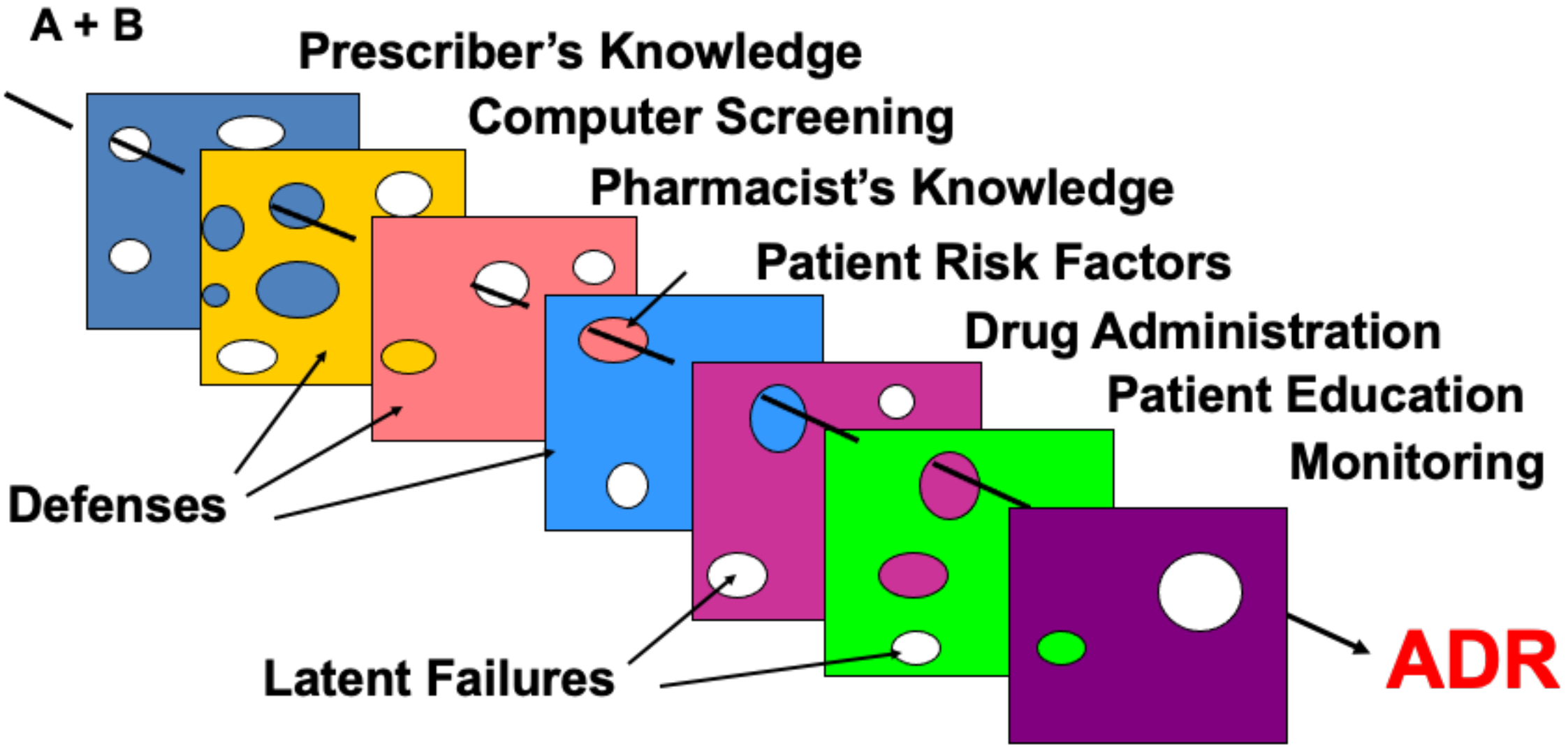
Clues About the Frequency of Harm

- Clinically important events attributable to drug-drug interactions:[1]
  - 5.3% – 14.3% of inpatients
  - 231,000 US emergency department visits
- Hospital admissions associated with an adverse drug event attributable to drug-drug interactions:[2]
  - 22.2% (interquartile range 16.6% – 36.0%)

[1] Magro L, Moretti U, Leone R. Epidemiology and characteristics of adverse drug reactions caused by drug-drug interactions. *Expert Opin Drug Saf*. 2012;11(1):83-94. doi:10.1517/14740338.2012.631910

[2] Dechanont S, Maphanta S, Butthum B, Kongkaew C. Hospital admissions/visits associated with drug-drug interactions: a systematic review and meta-analysis. Pharmacoepidemiol Drug Saf. 2014;23(5):489-497. doi:10.1002/pds.3592.

“When the Holes Line Up”



Hansten PD, Horn JR. Modified from: James Reason, Human Error, 1990

Prescribers' PDDI Knowledge

Prescriber knowledge is often lacking

- 12,500 United States prescribers correctly identified 42.7% of 14 drug pairs[1]
- 281 Iranian medical residents correctly classified only 41% (5.7/14) of 14 drug pairs[2]
- Mean number of correct responses from 244 Turkish physicians regarding the clinical significance of the 7 COVID-19 therapy related DDIs was 2.04 (±1.31)[3]

[1] Ko et al. *Drug Saf.* 2008;31(6):525 – 536.
[2] Nabovati et al. International journal of clinical pharmacy 39.3 (2017): 560 – 568.
[3] Sürmelioğlu et al. Postgraduate Medicine (2020): 1 – 5.

Does CDS Work?

Systems that provide PDDI alerts at the point of care often alert to PDDIs that have little potential clinical significance

- **Frustrating clinicians**: Clinicians override up to 90% of potential DDI alerts, primarily because clinicians do not consider the alerts to be relevant.
- **Can lead to inappropriate responses**: 87.3% of high-priority alerts were overridden in a 1-year sample of inpatient and outpatient data from a large academic health system; less than half (45.4%) of the overrides were considered appropriate

Edrees H, Amato MG, Wong A, Seger DL, Bates DW. High-priority drug-drug interaction clinical decision support overrides in a newly implemented commercial computerized provider order-entry system: Override appropriateness and adverse drug events. J Am Med Inform Assoc. 2020;27(6):893-900. doi:10.1093/jamia/ocaa034

Key Point

PDDI clinical decision support is currently sensitive but not precise; alerts are more effective when they consider the specific patient context

- Daniels *et al*.[1] observed a reduction in the override rate from 93.9% to 46.8% after making nearly a third (30.2%) of DDI alerts more contextual and suppressing another 16.5% of alerts.

[1] Daniels CC, Burlison JD, Baker DK, et al. Optimizing Drug-Drug Interaction Alerts Using a Multidimensional Approach. Pediatrics. 2019;143(3). doi:10.1542/peds.2017-4111

What Does a Contextualized PDDI Algorithm Look Like?

- See the CDS Connect Repository
  - Warfarin – NSAIDS: https://cds.ahrq.gov/cdsconnect/artifact/contextual-drug-interaction-decision-support-algorithm-warfarin-nonsteroidal
  - Warfarin – antidepressants: https://cds.ahrq.gov/cdsconnect/artifact/contextual-drug-interaction-decision-support-algorithm-warfarin-antidepressants
- Others in the process of release to CDS Connect
  - ddi-cds.org

Authoring Structured PDDI CDS

CDS Hooks in the Prescribing Workflow

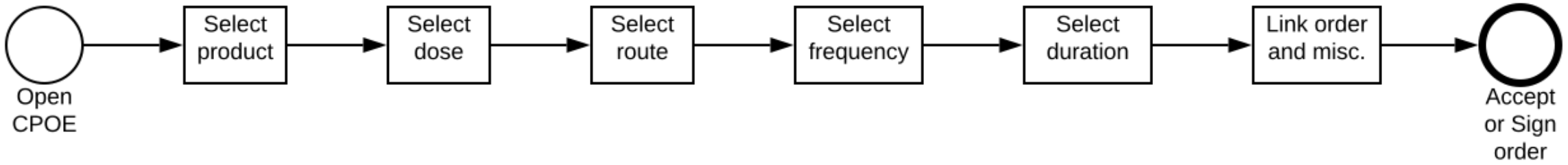
- Patient-view hook
  - Clinician
  - Shared decision making
- Order-select, order-sign hooks
  - Clinician

Patient View

- Short card summary of PDDIs
  - Can be actionable from the card
- SMART App link
  - Many PDDI situations require clinician input to arrive at the appropriate action
  - Shared decision making

Order-Select/Order-Sign

- Clinician-facing CDS
  - Order-select
    - Early in the prescribing workflow
      - Less cognitive burden than at order-sign?
  - Order-sign
    - Last step in the prescribing workflow



order-select — — — — — — — — — — — — → order-sign

Additional Requirements?

- Ability to test the rules
  - Retrospectively
  - Prospectively

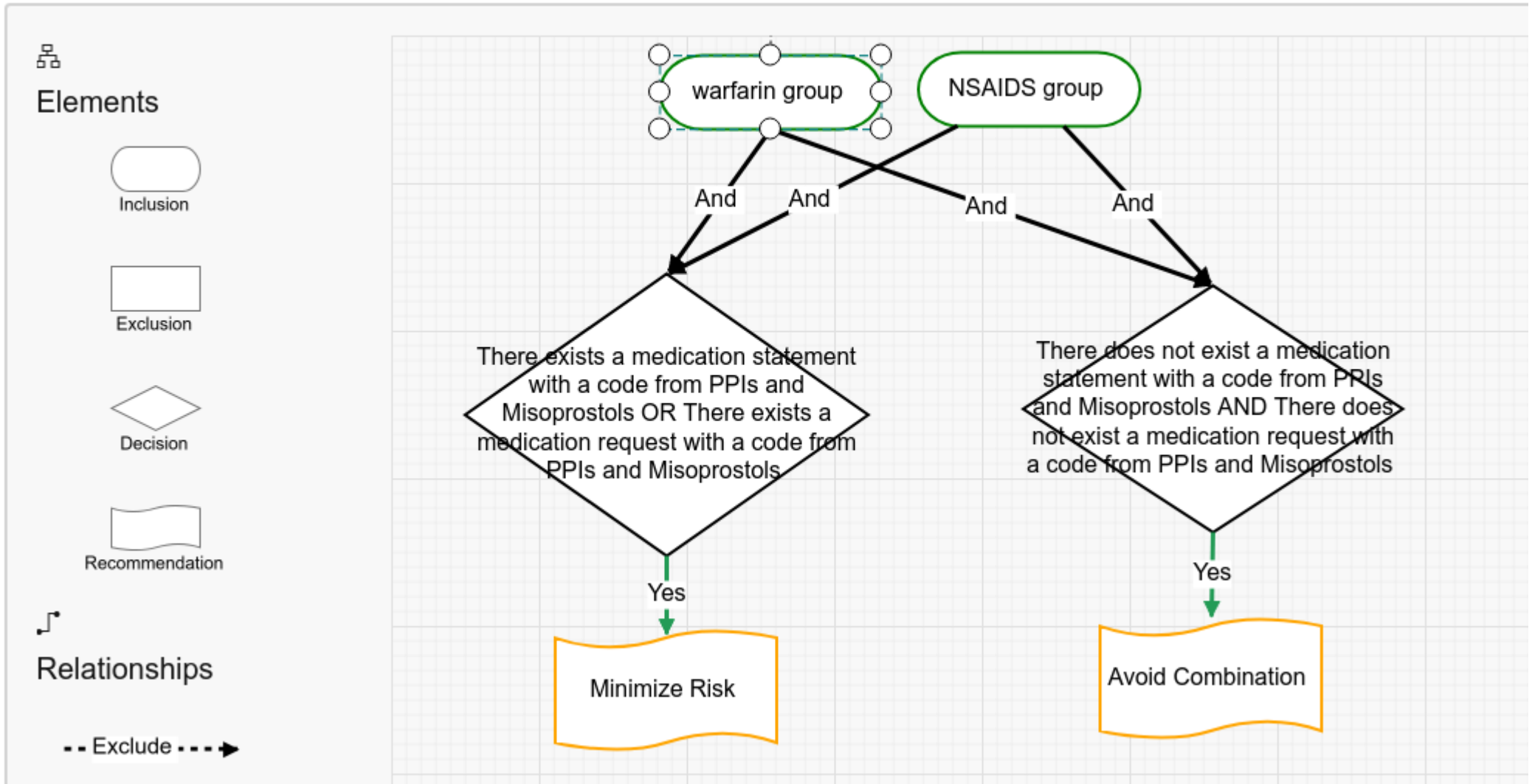
- Simple to author
  - Most authors are not knowledgeable about FHIR and need some help to pick the correct resources

Authoring PDDI CDS Rules (1/5)

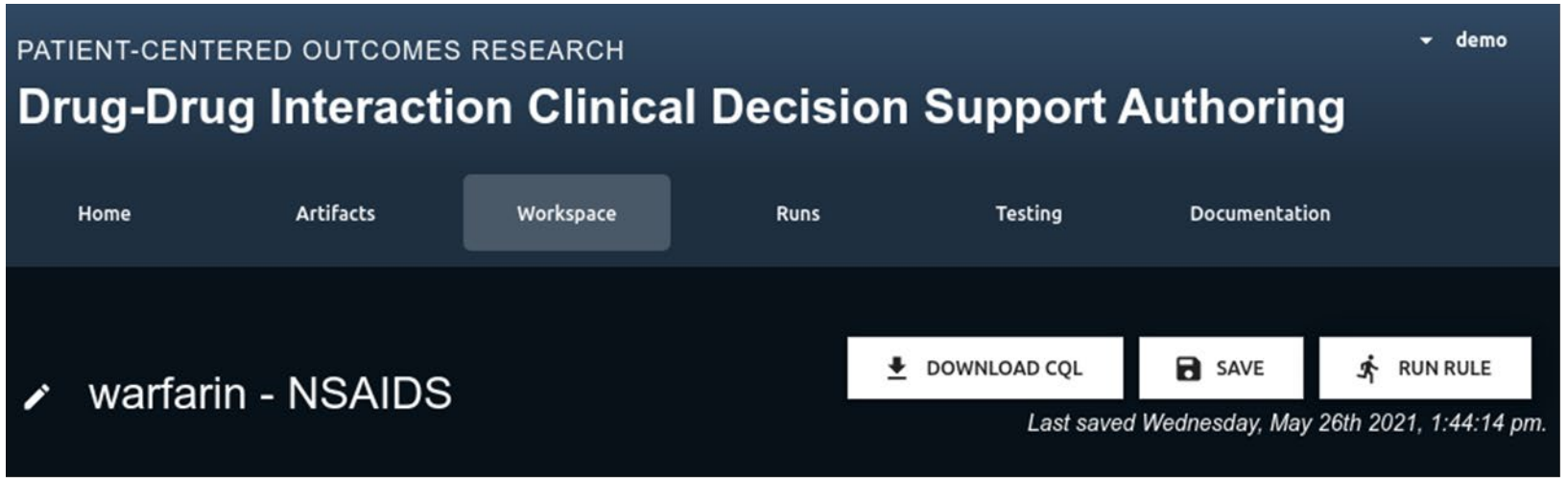
https://authoring.ddi-cds.org/authoring/

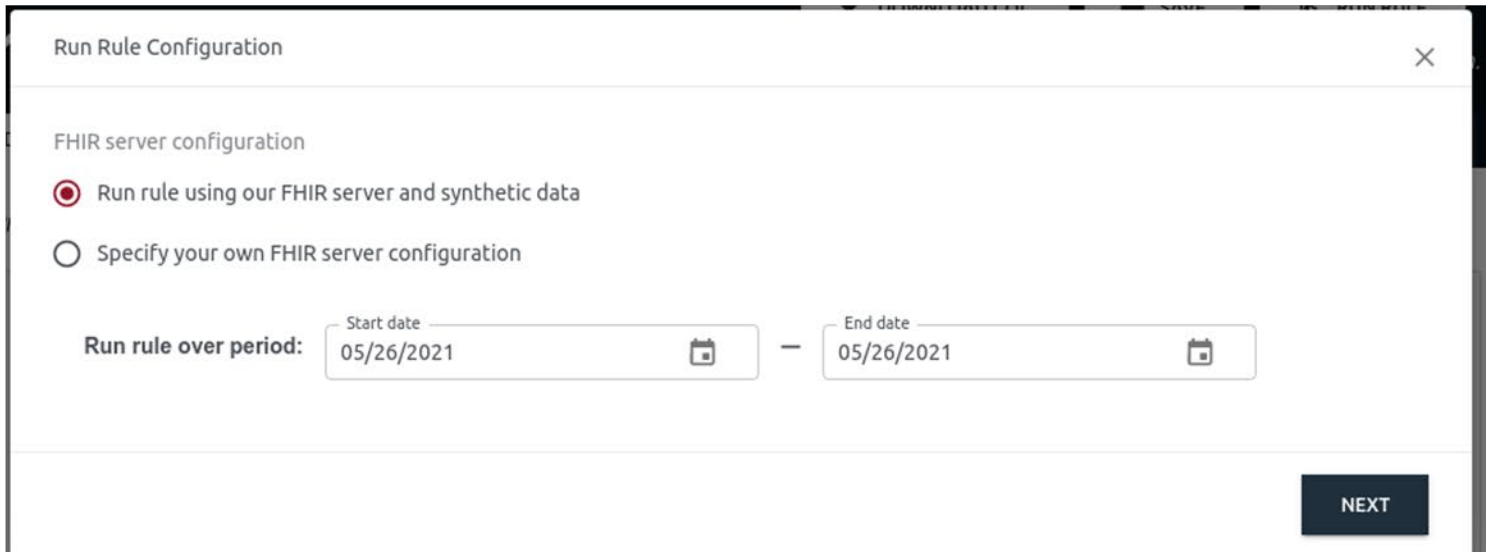
Authoring PDDI CDS Rules (2/5)

Build a decision diagram.

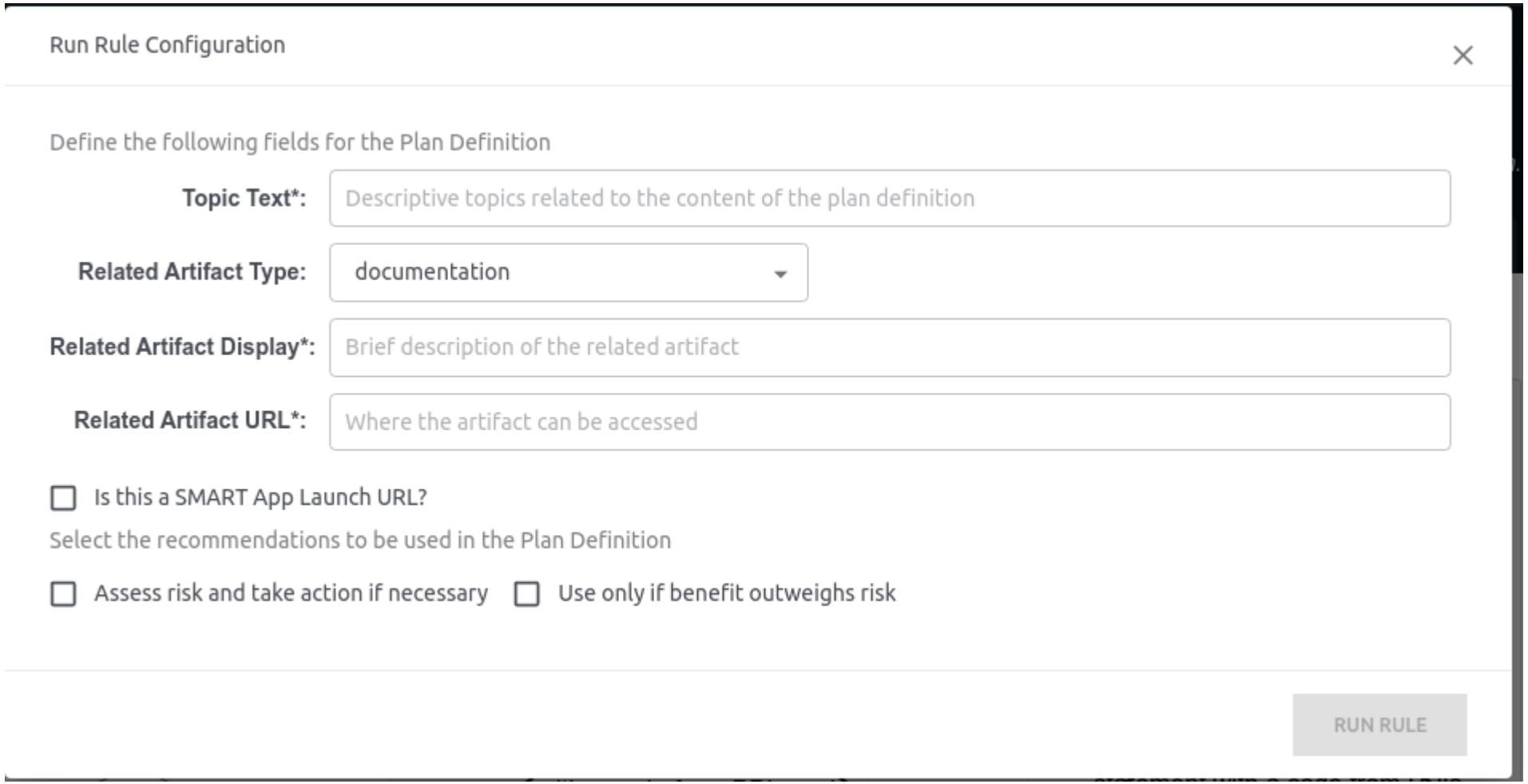


Authoring PDDI CDS Rules (3/5)





Authoring PDDI CDS rules (4/5)



Authoring PDDI CDS rules (5/5)

Warfarin - NSAIDs	Alerts 6/1/2021 - 6/3/2021	
	Patients	15
	Total	12
	Minimize Risk	6
	Avoid Combination	2

Warfarin - NSAIDs	Alerts 6/1/2021 - 6/3/2021	
	Patient 1	Minimize Risk
	Patient 2	Avoid Combination
	Patient 3	No alert

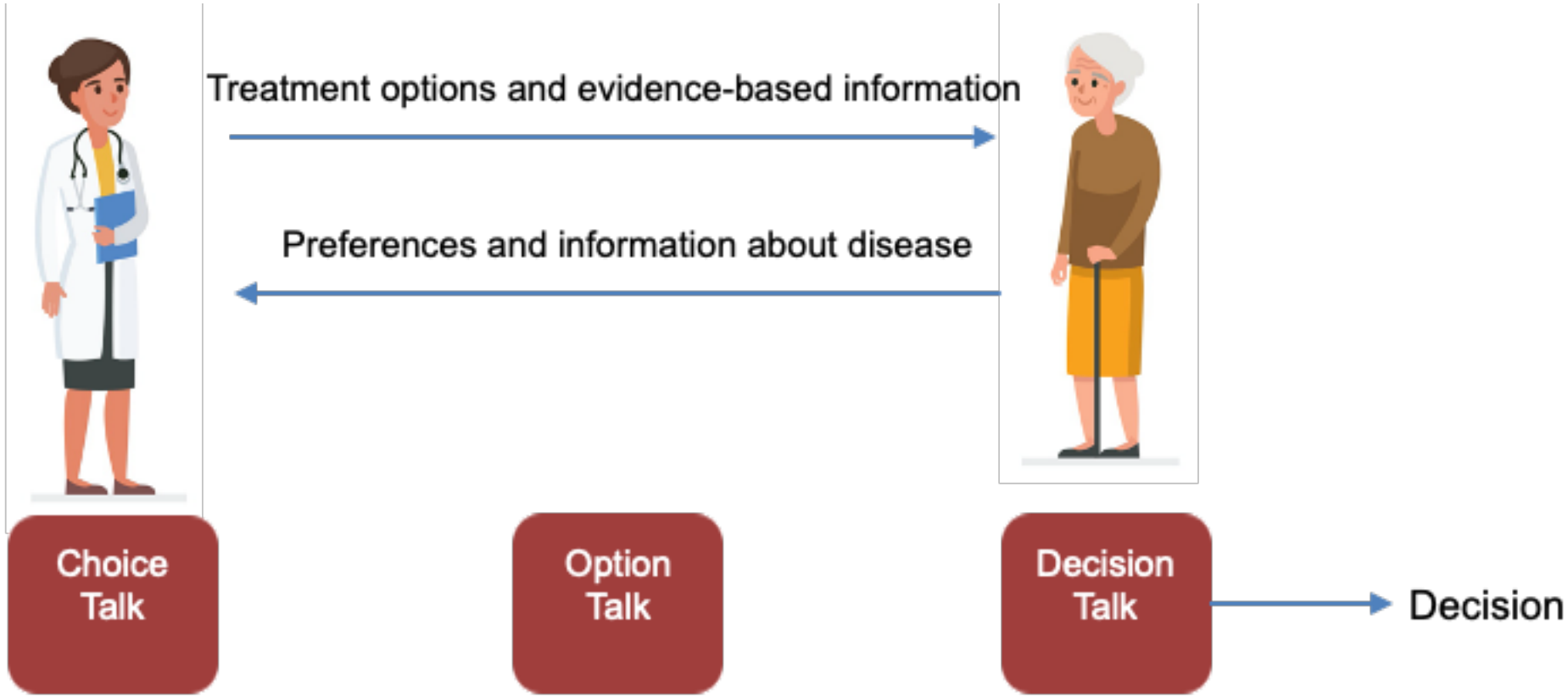
Shared Decision Making via DDInteract™

Shared Decision Making with DDIs

- DDInteract
  - Novel SDM app to improve clinician and patient understanding of risk of harm due to exposure to select potential DDIs.

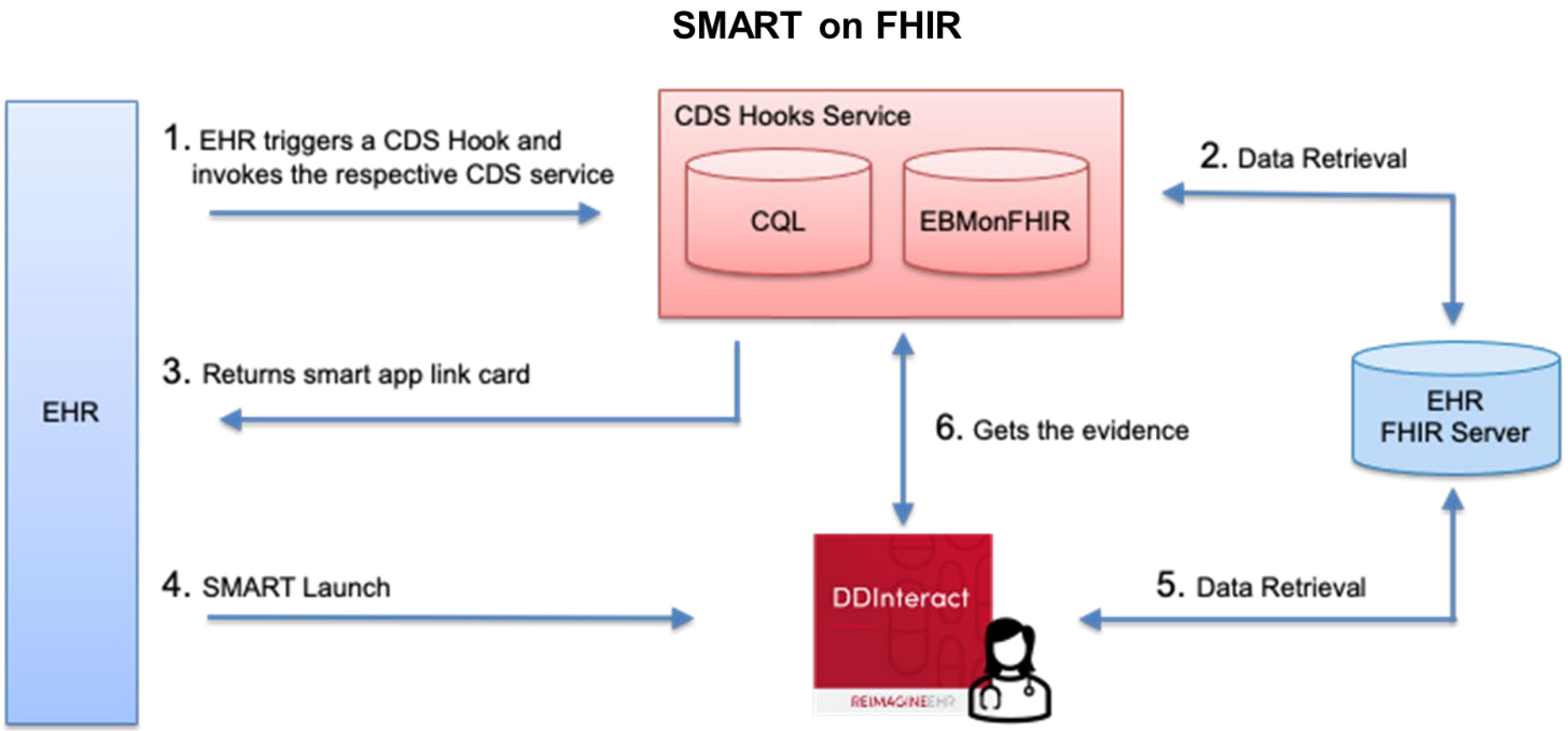
Shared Decision Making

Occurs when a healthcare provider and a patient work together to make a care decision that is best for the patient.

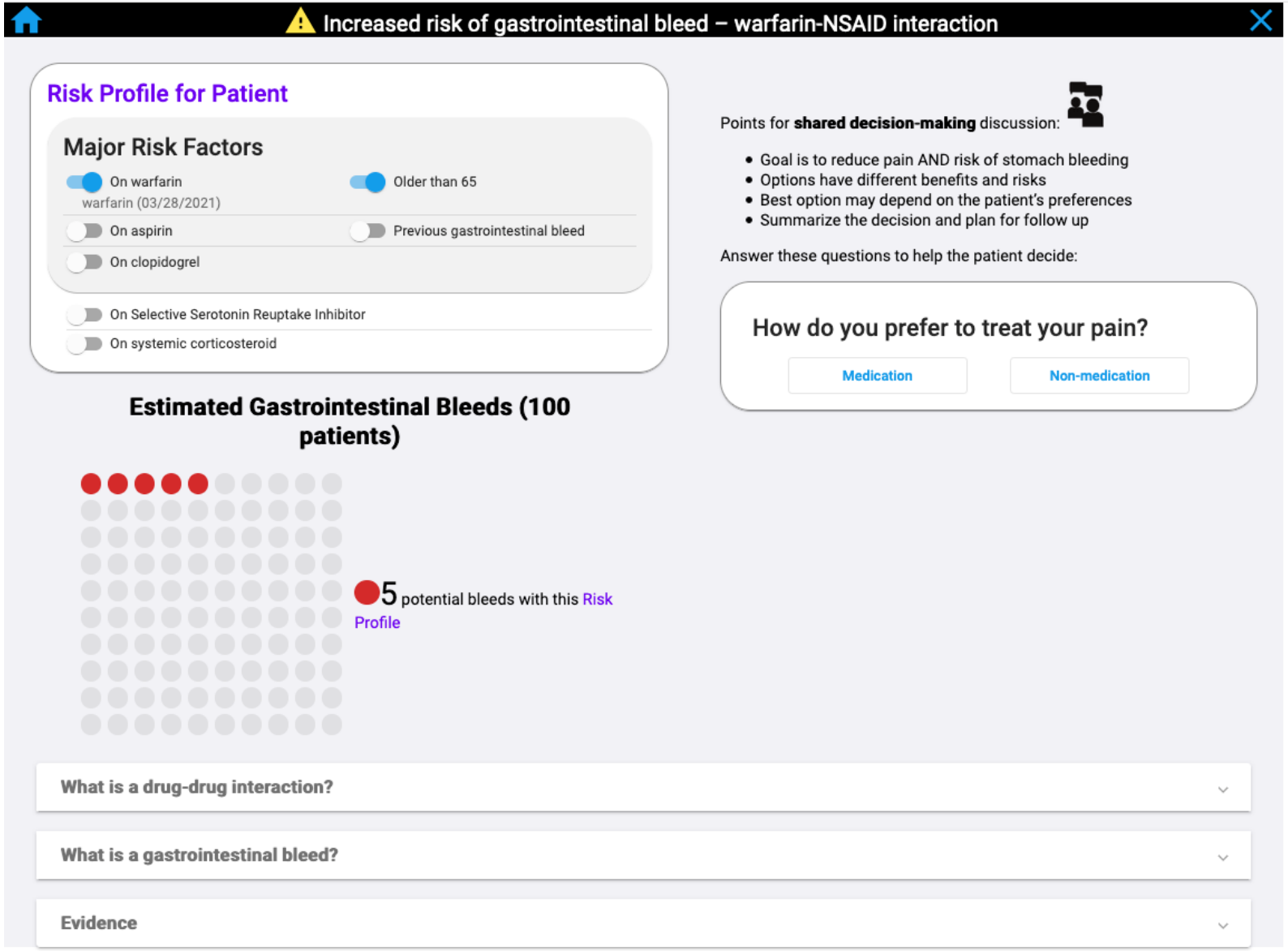


Elwyn G et al. Shared decision making: a model for clinical practice. *J Gen Intern Med*. 2012

Theoretical Connectivity

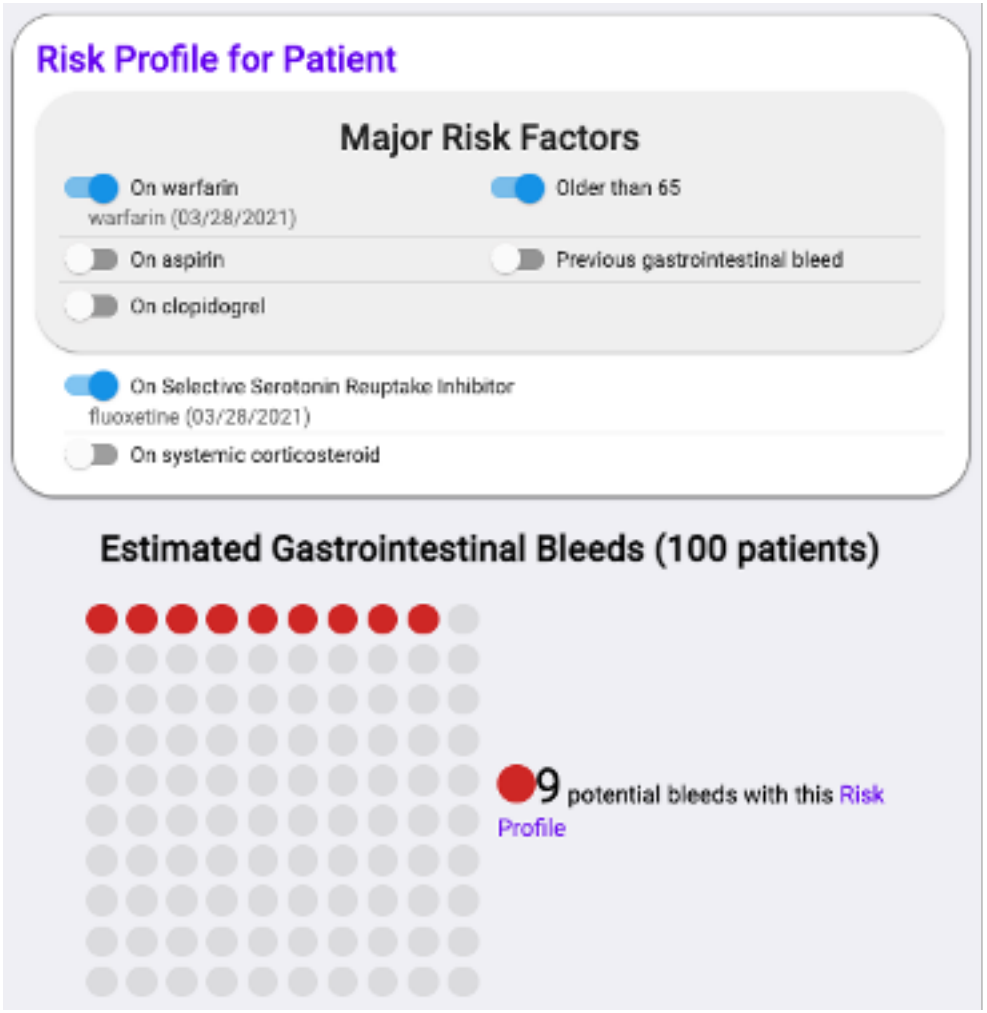


Overall View



Design

Primary Information Tab



Patient Risk Factors

Visual Display of Patient Risk

Shared Decision Making Attributes (1/2)

Points for **shared decision-making** discussion:

- Goal is to reduce pain AND risk of stomach bleeding
- Options have different benefits and risks
- Best option may depend on the patient's preferences
- Summarize the decision and plan for follow up

Answer these questions to help the patient decide:

How do you prefer to treat your pain?

Medication | Non-medication

Shared Decision Making Attributes (2/2)

Points for **shared decision-making** discussion:

- Goal is to reduce pain AND risk of stomach bleeding
- Options have different benefits and risks
- Best option may depend on the patient's preferences
- Summarize the decision and plan for follow up

Answer these questions to help the patient decide:

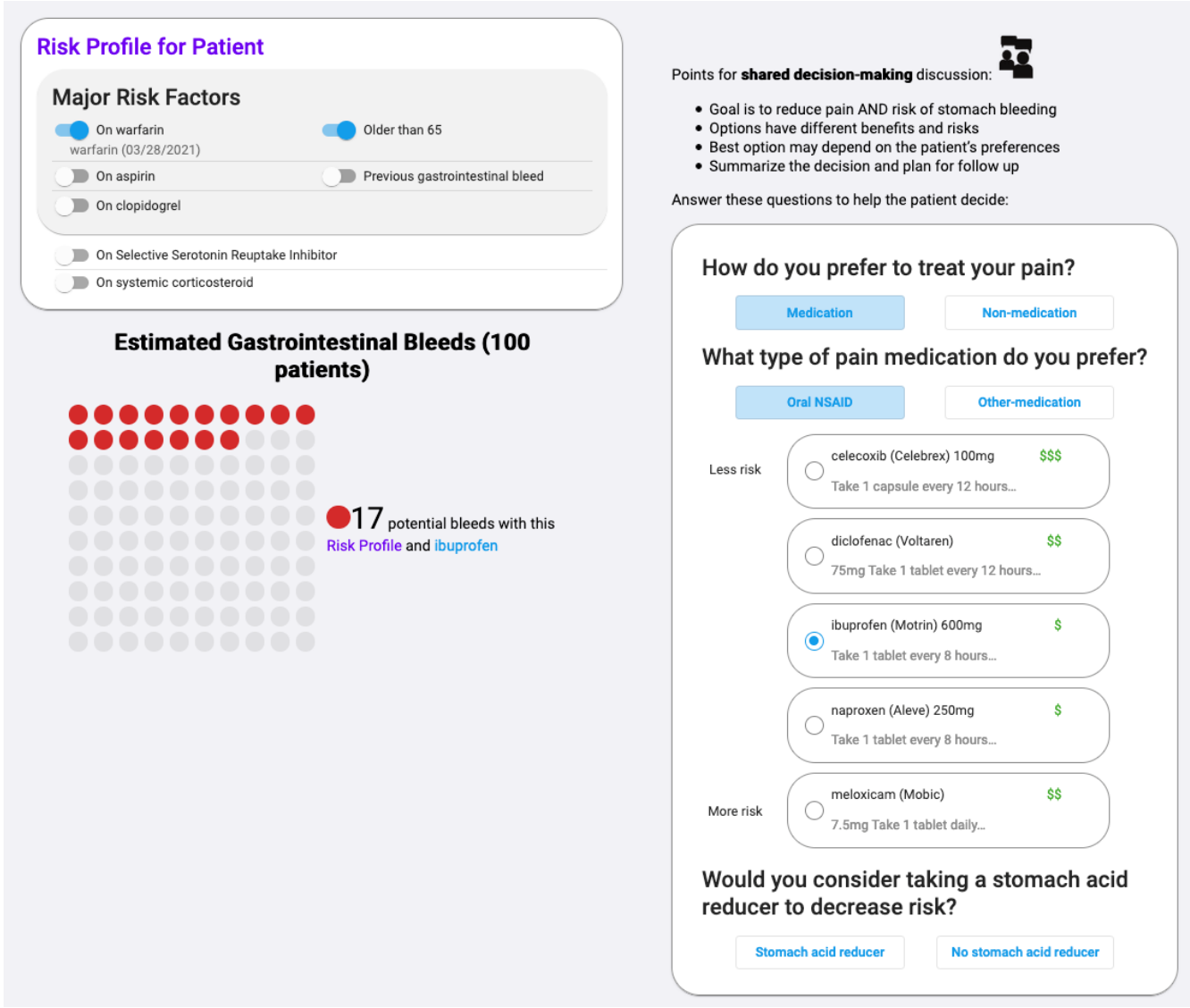
How do you prefer to treat your pain?

Medication | Non-medication

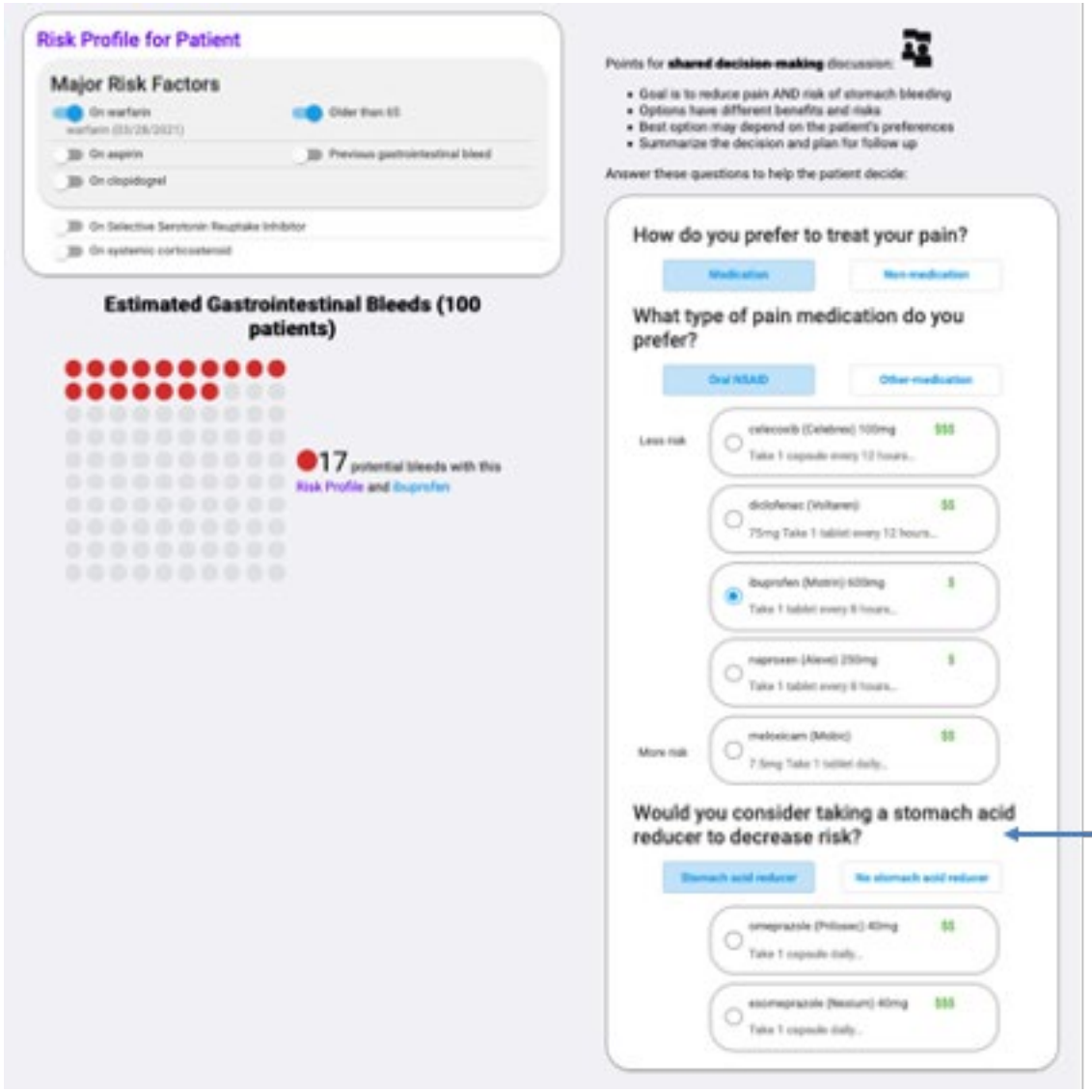
What type of pain medication do you prefer?

Oral NSAID | Other-medication

Shared Decision Making Screenshot

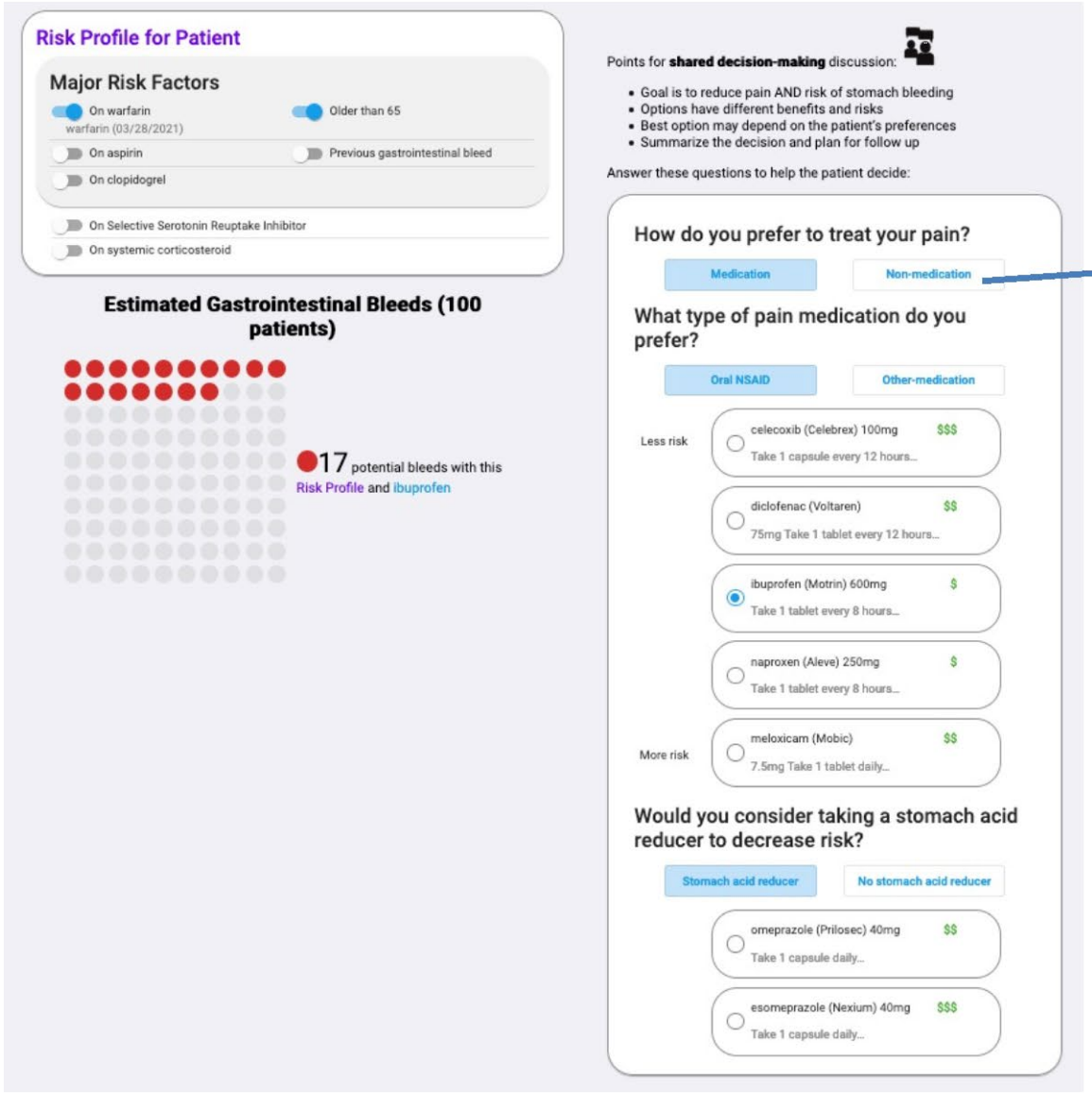


Screenshot 2



Methods to Reduce Risk

Non-Medication Treatments



Alternative Treatments

How do you prefer to treat your pain?

Medication | Non-medication

- **Acupuncture**
- **Biofeedback**
- **Electrical Stimulation**
- **Exercise/Stretching**
- **Massage Therapy**
- **Meditation**
- **Physical Therapy**
- **Positive Psychology/Spiritual/Meaningfulness**
- **Psychotherapy**
- **Relaxation Therapy**
- **Sleep Habits**
- **Surgery (specific cases)**
- **Weight Loss (specific cases)**

For further information visit: MedlinePlus.

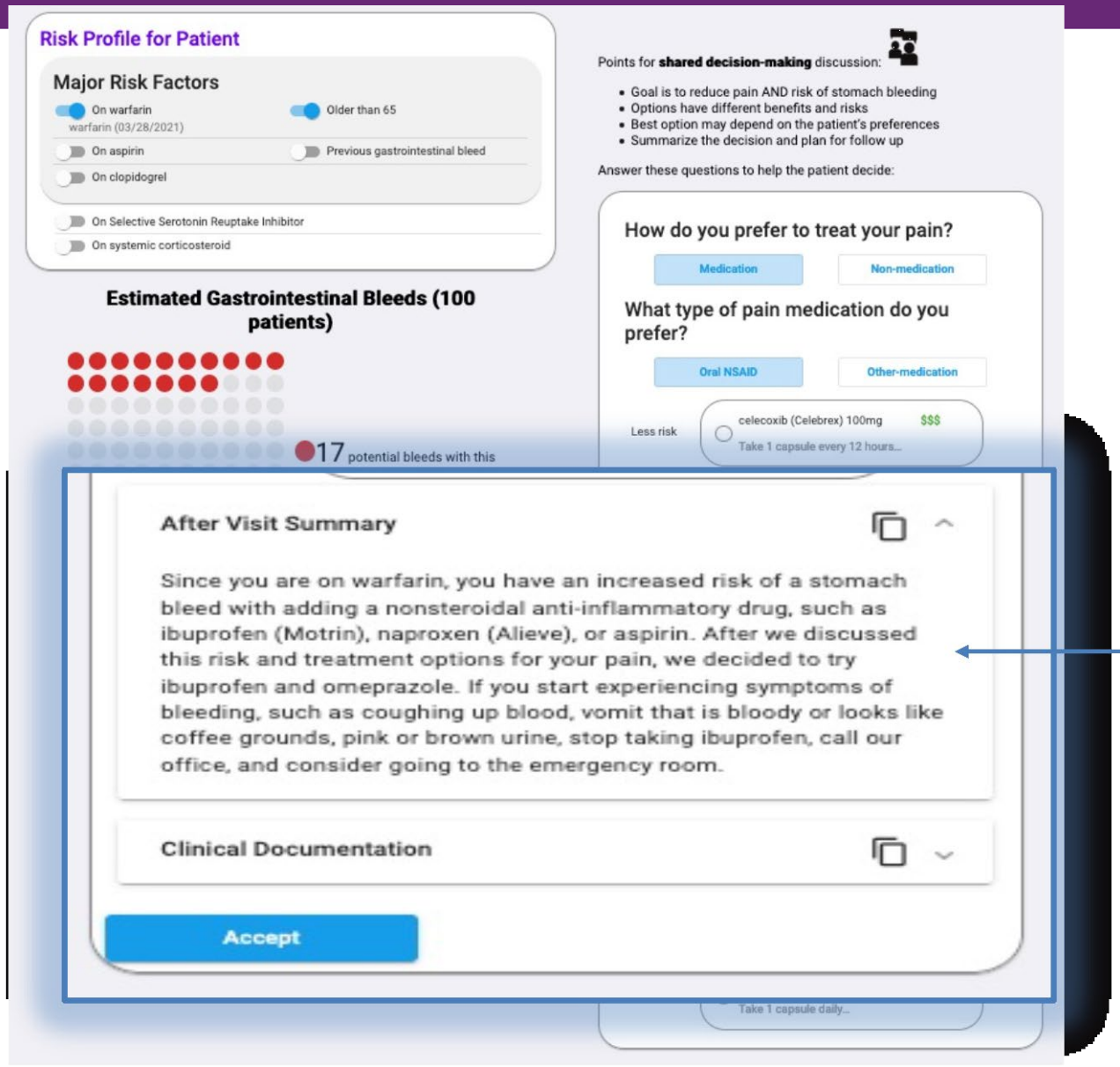
After Visit Summary

Since you are on warfarin, you have an increased risk of a stomach bleed with adding a nonsteroidal anti-inflammatory drug, such as ibuprofen (Motrin), naproxen (Alieve), or aspirin. After we discussed this risk and treatment options for your pain, we decided to try an alternative treatment without medications. If you decide you need pain medication before we reassess, you can use acetaminophen (Tylenol) 250mg 1-2 tablets every 6 hours as needed for pain.

Clinical Documentation

Accept

Clincal Summary for Chart



Clinical Summary for Chart

Additional Information (1/4)

- What is a drug-drug interaction?
- What is a gastrointestinal bleed?
- Evidence

Additional Information (2/4)

What is a drug-drug interaction?

Wha

Evi

What is a drug-drug interaction?

- When two or more drugs react with each other and cause unwanted side effects
- Warfarin (Coumadin) and NSAIDS (nonsteroidal anti-inflammatory drugs) increases your risk of stomach bleeding

warfarin

ibuprofen

Additional Information (3/4)

What is a drug-drug interaction?

What is a gastrointestinal bleed?

Evidence

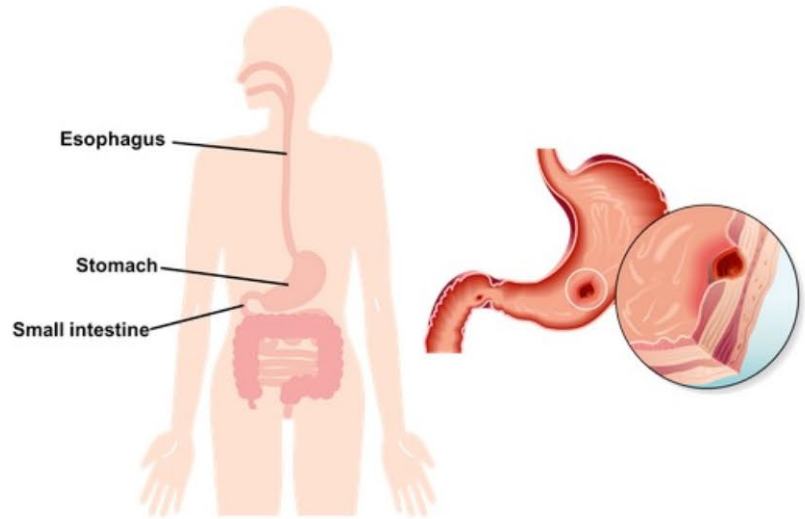
What is a gastrointestinal bleed?

Bleeding that occurs anywhere in the digestive tract, from the esophagus to the rectum.

Symptoms may include:

- Vomiting blood or something that looks like coffee grounds
- Melena: dark and tarry-appearing stools with a distinctive smell
- Feeling weak, light-headed, or woozy
- Rapid heartbeat
- Belly cramps or pain

Parts of your body that are most at risk for bleeding from a drug interaction include:



Additional Information (4/4)

What is a drug-drug interaction?

What is a gastrointestinal bleed?

Evidence

FORMULA

Risk

Age > 65 years = 2.5
On aspirin = 1.55
On clopidogrel = 3.66
On ssri = 2
On corticosteroid = 1.4
Hx of GI bleeding = 5
With stomach acid reducer = 0.24

Equation

$$Pr(Bleeding) = e^{Y_i} \div (1 + e^{Y_i})$$

$$Y_i = \beta_0 + \beta_i X_i + \varepsilon_i$$

Y_i = alpha + 0.91 * age + 0.44 * asa + 1.29 * clop + 0.69 * ssri + 0.33 * cortico + 1.61 * gibleed + 1.10 * cele + 1.10 * dico + 1.38 * ibup + 2.19 * indo + 2.19 * keto + 2.89 * ketr + 2.08 * napr + 2.08 * melo + 2.64 * piro + (-1.42) * ppi

This risk score has not been externally validated.

REFERENCES

Chen WC, Chen YH, Hsu PI, Tsay FW, Chan HH, Cheng JS, Lai KH. Gastrointestinal hemorrhage in warfarin anticoagulated patients: incidence, risk factor, management, and outcome. Biomed Res Int. 2014;2014:463767. doi: 10.1155/2014/463767. Epub 2014 May 29. PMID: 24987683; PMCID: PMC4059852.

Ray WA, Chung CP, Murray KT, Smalley WE, Daugherty JR, Dupont WD, Stein CM. Association of Proton Pump Inhibitors With Reduced Risk of Warfarin-Related Serious Upper Gastrointestinal Bleeding. Gastroenterology. 2016 Dec;151(6):1105-1112.e10. doi: 10.1053/j.gastro.2016.08.054. Epub 2016 Sep 14. PMID: 27639805; PMCID: PMC5124401.

Try DDInteract! (1/2)

- https://ddi-cds.org/apps/

Try DDInteract! (2/2)

Warfarin-NSAIDs Drug Interaction App (DDInteract™)

Click here to watch watch a short **video** that explains how the app was designed to work.

- You can demo the app by:
  - Running it like a risk calculator **Launch**
- Selecting any of the following patient profiles
  - Patient born in 1970 and taking warfarin 4 MG tablet, sulindac 200 MG tablet, and spironolactone 100 MG tablet – **Launch**
  - Patient born in 1952 and taking warfarin 4 MG tablet and sulindac 200 MG tablet with a history of GI bleeding – **Launch**
  - Patient born in 1940 and taking warfarin 10 MG tablet, prednisone 20 MG tablet, and ketorolac tromethamine 10 MG tablet – **Launch**
  - Patient born in 1970 and taking warfarin 10 MG tablet and ketorolac tromethamine 10 MG tablet – **Launch**
  - Patient born in 1952 and taking 4 MG warfarin tablet and a topical diclofenac lotion – **Launch**

Please provide us with your feedback!!

We are interested in your opinions about our tool. Below is a link to a confidential survey. At the end of the survey you have the option to enter a drawing for one of ten $100 Amazon gift card! (drawing open to the first 100 participants)

https://www.surveymonkey.com/r/5BC32WX

We would welcome any other comments you have. You can also email us at **info@ddi-cds.org**

DDInteract™* is a shared decision making tool designed to assist both prescribers and patients understand the risks of bleeding while taking warfarin with and without NSAIDs. The app was designed with input from physicians, pharmacists, patients, and human factors researchers. *Trademark pending

Summary

- First authoring-to-service environment for PDDI CDS artifact development

- DDInteract is a novel SDM tool for managing drug-drug interactions
  - ► App-based approach for the last mile of meaningful CDS for drug safety

Discussion

WHAT'S NEW WITH CDS CONNECT

Matt Coarr and Chris Moesel, MITRE

Updates and New Features

- **Authoring Tool**
  - Support for using base elements, parameters, and external CQL as arguments to external CQL functions
  - Support for Strength of Recommendation and Quality of Evidence in CPG form
  - Updates to design and interaction of Value Set Authority Center integration
  - Visual error indicators and content indicators on tabs in Workspace
  - “Sticky” tabs so authors always know their context (e.g., Inclusion, Exclusions)
  - Bug fixes and continued updates to support reusability and maintainability

- **Repository**
  - API update for related artifacts deployed (now returning title, ID, and URL for each related artifact)
  - UI changes in progress
  - CPG-on-FHIR work continues
  - User documentation update continues
  - Updated environments to PHP 7.4
  - Software updates and security patches — In progress: Drupal 9 and Acquia Dev Desktop replacement
  - Technical support for Repository contributors

Link to CDS Connect: https://cds.ahrq.gov/cdsconnect

ANNOUNCEMENTS, OPEN DISCUSSION AND CLOSE-OUT

Maria Michaels
Office of Public Health Scientific Services
Centers for Disease Control and Prevention