DDInteract[™]

A Novel Drug-Drug Interaction Tool for Patients Taking Oral Anticoagulants







WHAT IS DDINTERACT?



- A tool for clinicians for patients who take oral anticoagulants including apixaban, dabigatran, edoxaban, rivaroxaban, and warfarin
- Shows the risk of gastrointestinal bleeding when these patients take NSAIDs and/or antidepressants
- Utilizes current medications and diagnosis information to calculate risk for gastrointestinal bleeding
- Available in EPIC as on-demand (Does not replace current DDI alerts)



Anticoagulant Drug Interactions

Bleeding Risk for Antidepressant and Pain Medications

Higher

Risk

1.01

1.31

1.31

1.34

1.56

1.56

3.12

3.12

3.12

5.96

6.52

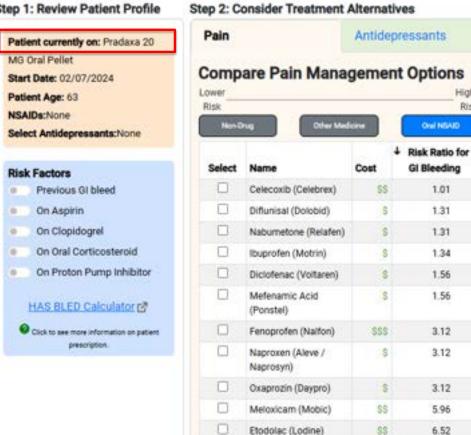
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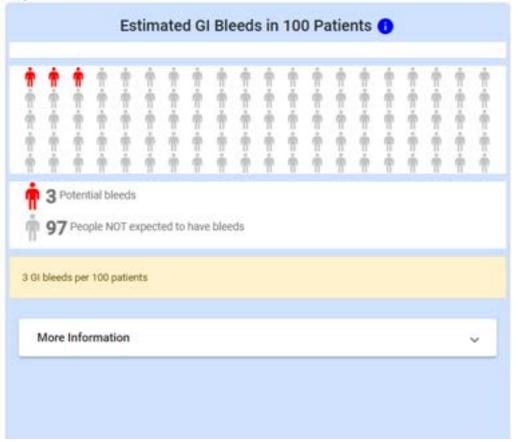
Shared Decision-Making Tips (1)

Step 1: Review Patient Profile



Indomethacin (Indocin)

Step 3: Evaluate Results

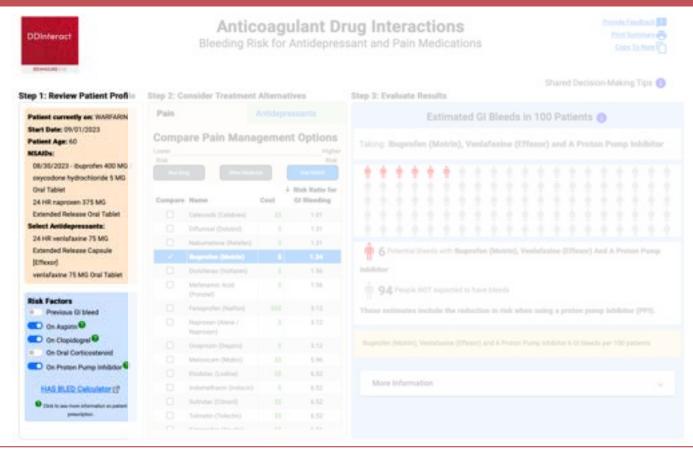


A STEP-BY-STEP OVERVIEW

DDInteract

REIMAGINETHE





STEP 1: REVIEW PATIENT PROFILE

DDInteract uses patient-specific EHR information to calculate risk of GI bleeding for patients taking NSAIDs and/or antidepressants

Step 1: Review Patient Profile

Patient currently on: WARFARIN

Start Date: 09/01/2023

Patient Age: 60

NSAIDs:

08/30/2023 - ibuprofen 400 MG /

oxycodone hydrochloride 5 MG

Oral Tablet

24 HR naproxen 375 MG

Extended Release Oral Tablet

Select Antidepressants:

24 HR venlafaxine 75 MG

Extended Release Capsule

[Effexor]

venlafaxine 75 MG Oral Tablet

Risk Factors

Previous GI bleed

On Aspirin

On Clopidogrel

On Oral Corticosteroid

On Proton Pump Inhibitor 🛭

HAS BLED Calculator

Click to see more information on patient prescription.



STEP 1: REVIEW PATIENT PROFILE

- Displays patient information retrieved from the electronic health record, including age and concomitant medications
- Lists any current NSAIDs and antidepressants the patient is taking

Step 1: Review Patient Profile

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Patient Age: 60

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STEP 1: REVIEW PATIENT PROFILE

Incorporates the following risk factors:

- Age
- Previous GI Bleed
- On Aspirin
- On Clopidogrel
- On Oral Corticosteroids
- On Proton Pump Inhibitor (PPI)

Clinicians can toggle risk factors on and off to update the information

Link to HAS BLED calculator at bottom



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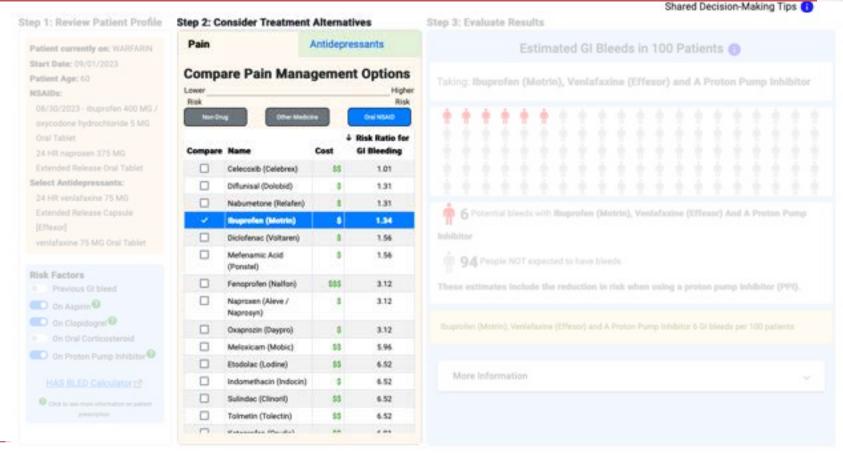


A STEP-BY-STEP OVERVIEW

DDInteract

REIMAGINETHE

Step 2: Consider Treatment Alternatives

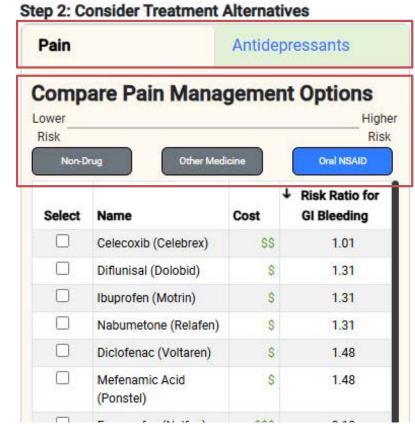




Contains two main tabs:

- 1. Pain Management Options
- 2. Antidepressant Options

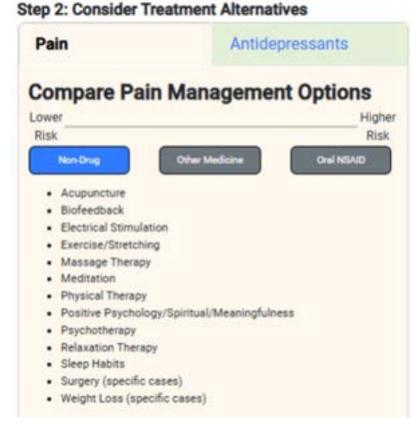
Three sub-menu tabs show treatment alternatives from lower to higher risk





Pain Management Options (3 tabs)

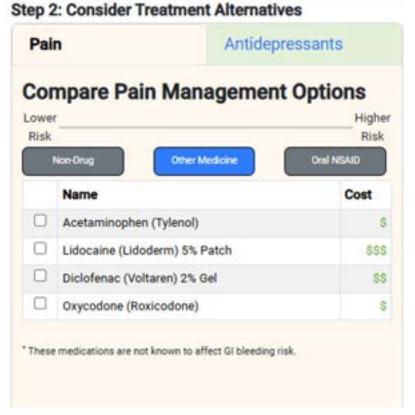
 Non-Drug Options: Lists alternatives that do not involve medication such as acupuncture and biofeedback





Pain Management Options

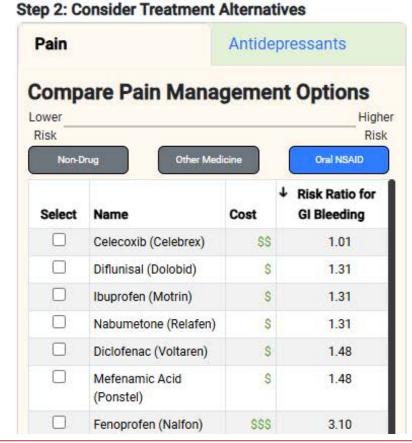
 Other Medicine: Lists medications that do not increase GI bleeding risk, such as Tylenol and topical medications





Pain Management Options

 Oral NSAIDs: Displays a list of NSAIDs with their cost and risk ratios for GI bleeding





Pain Management Options

 Oral NSAIDs: Displays a list of NSAIDs with their cost and risk ratios for GI bleeding

Can sort list by:

- Generic product name
- Cost
- GI bleeding risk





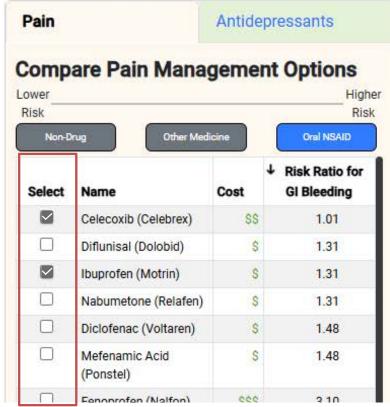
Pain Management Options

 Oral NSAIDs: Displays a list of NSAIDs with their cost and risk ratios for GI bleeding

Selection column:

 Compare up to 2 medications, showing the GI bleeding risk for selected medications

Step 2: Consider Treatment Alternatives





Antidepressant Options

Allows sorting of lists by

- GI bleeding risk
- Product name
- Cost

Selection column:

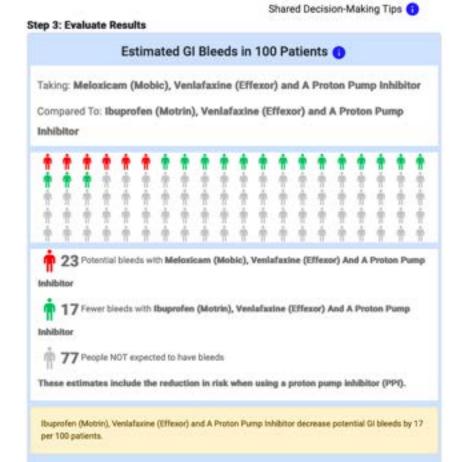
 Compare up to 2 medications, showing the GI bleeding risk for selected medications

Pain		Antidepressants	
Compare Antidepressant Options			
Select	Name	Cost	◆ Risk Ratio for GI Bleeding
	Bupropion (Wellbutrin)	\$	1.00
	Mirtazapine (Remeron)	\$	1.08
	Duloxetine (Cymbalta)	\$	1.24
	Fluvoxamine (Luvox)	S	1.25
	Sertraline (Zoloft)	\$	1.29
	Desvenlafaxine (Pristiq)	SS	1.37
	Venlafaxine (Effexor)	SS	1.37
\checkmark	Escitalopram (Lexapro)	\$	1.44
	Paroxetine (Paxel)	S	1.45
	Citalopram (Celexa)	\$	1.61
	Fluoxetine (Prozac)	S	1.62

Sten 2: Consider Treatment Alternatives

STEP 3: EVALUATE RESULTS

- Visually presents the estimated GI bleeding risk for 100 patients based on the selected medication options
- The screen compares the risk between two medications, showing how the choice affects patient outcomes when a Proton Pump Inhibitor (PPI) is also considered



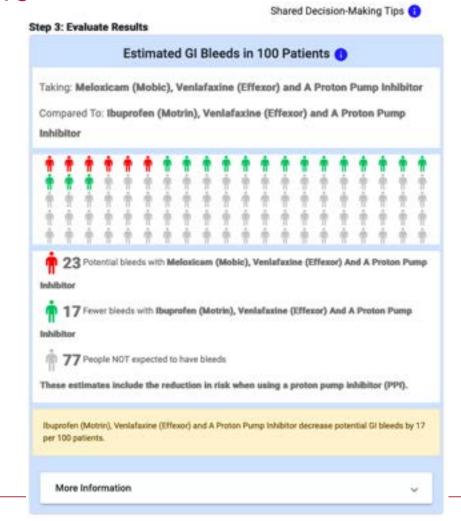
More Information



STEP 3: EVALUATE RESULTS

Color Coding:

- Red figures show the number of patients expected to experience GI bleeding with the first medication
- Green figures represent the reduction in bleeds when switching to a safer second medication
- Grey figures show the number of patients not expected to bleed



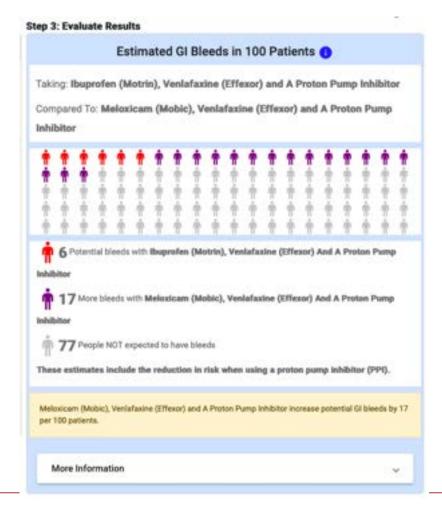


STEP 3: EVALUATE RESULTS

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 Purple Figures represent the increase in bleeds when switching to a higher-risk medication

Color Coding:







Anticoagulant Drug Interactions

Bleeding Risk for Antidepressant and Pain Medications

Higher

Risk

1.34

1.48

1.56

3.10

3.10

3.12

5.96

6.52

6.70

6.70

6.70

6.91

11.59

22.51



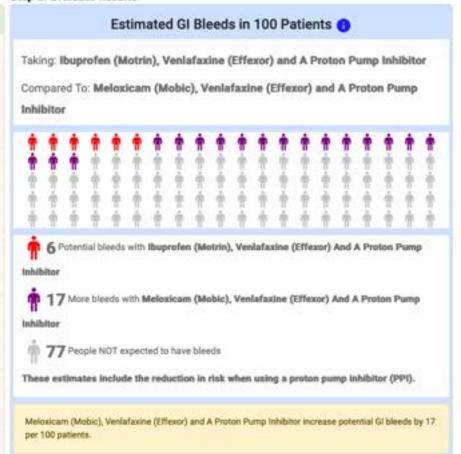
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Step 1: Review Patient Profile

Pain Antidepressants Patient currently on: WARFARIN Start Date: 09/01/2023 Compare Pain Management Options Patient Age: 60 NSAIDs: Risk 08/30/2023 - ibuprofen 400 MG / CHAIN MAKE oxycodone hydrochloride 5 MG **Oral Tablet** + Risk Ratio for Compare Name Cost GI Bleeding 24 HR naproxen 375 MG **Buprofen (Motrin) Extended Release Oral Tablet** Select Antidepressants: Mefenamic Acid (Ponstel) 24 HR venlafaxine 75 MG Extended Release Capsule Diclofenac (Voltaren) [Effexor] Fenoprofen (Nalfon) venlafaxine 75 MG Oral Tablet Oxaprozin (Daypro) Naproxen (Aleve, **Risk Factors** Naprosyn) Previous GI bleed Meloxicam (Mobic) 88 On Aspirin® Indomethacin (Indocin) On Clopidogrel • Etodolac (Lodine) 88 On Oral Corticosteroid Sulindac (Clinoril) \$5 On Proton Pump Inhibitor Tolmetin (Tolectin) 88 Ketoprofen (Orudis) HAS BLED Calculator par Piroxicam (Feldene) 88 Click to see more information on patient Ketorolac (Toradol) 55

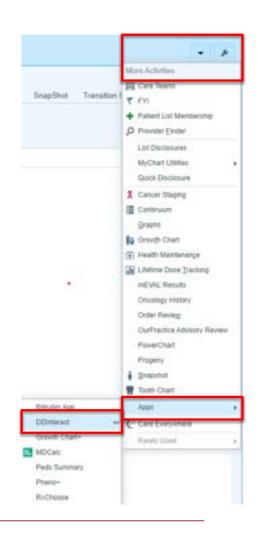
Step 2: Consider Treatment Alternatives

Step 3: Evaluate Results



HOW TO ACCESS DDINTERACT

- Log in to EPIC
- Navigate to the 'More Activities' menu:
 - At the top-right corner of the screen, click the dropdown arrow that shows additional options under 'More Activities'
- Locate 'Apps' under the 'More Activities' dropdown
- Select 'DDInteract' from the list of Apps



DDINTERACT LIMITATIONS





Medication Dose

- DDInteract does not consider the specific dose of a medication when assessing risk
- Existing literature fails to provide the risk for each product at the dose level

LIMITATIONS





Timing of the interaction

- DDInteract does not incorporate time to GI bleeding event
- Only 20% of the studies included time to event data, preventing us from incorporating time across all studies
- Harm from DDIs most commonly occurs early in the course of therapy, making the initial period particularly critical

LIMITATIONS





Focus on Specific Interactions:

- DDInteract does not encompass all possible drug-drug interactions
- Does not replace existing alerts
- Targeted Selection: focus on interactions between medications with known GI bleeding risks when used with oral anticoagulants
- Prioritizing High-Risk Interactions: addresses the most clinically significant risks that could impact patient safety

LIMITATIONS



Why do we just focus on gastrointestinal bleeding?

- Gastrointestinal bleeding is a common adverse event for patients taking oral anticoagulants
- This outcome is frequently studied because it is more common than other anatomical locations (such as intracranial)
- The evidence is more extensive for this outcome compared to other outcomes and some medications like NSAIDs are well-known for their effect on gastric mucosa

Summary



DDInteract: Personalized Risk Prediction for GI Bleeding

- Dynamic shared decision-making tool for assessing GI bleeding risk in patients on oral anticoagulants who use medicines for pain and depression
- Leverages patient-specific data from the EHR
- Focuses on common and clinically relevant drug-drug interactions with oral anticoagulants

Try DDInteract outside of Epic: https://prueba.bmi.utah.edu/ddinteract/



Identify risk factors



Search literature for evidence



Limit search to GI bleeds



Limit further to specific medications where appropriate



Estimate GI bleeding risk



Weight evidence of risk across all studies





RISK MODEL DEVELOPMENT





Comprehensive Review:

 Over 500 studies were reviewed to obtain accurate estimates of GI bleeding risk associated with each risk factor

 These studies provided the necessary data to ensure the risk model is based on robust and well-supported evidence

Prediction Model:

- Developed using the logarithm of the odds ratio (OR), similar to logistic regression, for each identified risk factor
- Designed to provide an overall risk estimate for an individual patient's GI bleeding

RISK MODEL DEVELOPMENT



Model Calibration:

The model was calibrated to predict GI bleeding events in patients receiving oral anticoagulants (OACs), even when no additional risk factors were present



OTHER RISK FACTORS NOT INCLUDED: COMORBIDITIES



Expert panel developed the algorithms used in DDInteract

Comorbidities such as renal and liver impairment, diabetes, and hypertension were not included in the algorithm



OTHER RISK FACTORS NOT INCLUDED: SMOKING AND ALCOHOL





Smoking and alcohol use are potential risk factors for GI bleeding, but historically were not routinely documented in electronic health records (EHRs)

Risk of GI bleeding will vary depending on amount consumed.

