

TruRISK

The Science Behind Personalized Medication Risk

The Same Drug Interaction May Not Mean the Same Risk for Every Patient

Traditional drug-interaction systems identify **known potential risks between medications**. That information is important—but it does not always tell the clinician how relevant that risk may be for the individual patient.

One reason is **drug exposure**.

Two patients can take the same medications at the same standard doses yet process and clear those medications differently. Genetics, other medications, enzyme inhibition or induction, phenoconversion, organ function, and other factors can alter the amount of drug to which a patient is exposed.

TruRISK adds this patient-specific pharmacokinetic context to established medication-risk information.

The Scientific Principle Is Straightforward

Many adverse drug effects are **dose- or exposure-dependent**.

When metabolism or clearance decreases, systemic exposure to a medication may increase. Increased exposure can, in appropriate circumstances, increase the likelihood or severity of concentration-dependent adverse effects.

This leads to an important clinical question:

If two medications have a known interaction or adverse-effect risk, shouldn't that risk deserve greater attention when the patient also has evidence suggesting increased exposure to one or both medications?

That is a central scientific premise behind TruRISK.

Consider Two Patients

Both patients take **Drug A + Drug B**, and the combination has an established risk for a particular adverse effect.

Patient 1

Drug A → expected processing and exposure

Drug B → expected processing and exposure

Known interaction remains clinically relevant.

Patient 2

Drug A → reduced functional metabolism → potentially increased exposure

Drug B → expected exposure

Same known interaction—but now there is an additional patient-specific pharmacokinetic reason for greater concern if the adverse effect is exposure-dependent.

The interaction did not change.

The patient did.

From Known Risk to Personalized Risk Context

TruRISK is designed to move medication-risk assessment beyond simply asking:

“Can these medications interact?”

It adds another question:

“Given how this patient may currently be processing these medications, which established risks may be more clinically relevant right now?”

The conceptual process is:

1. Identify Established Risk

Known drug-drug interactions, adverse-effect relationships, pharmacodynamic risks, disease-related risks, and other evidence-supported medication concerns are identified.

2. Add TruTYPE Pharmacokinetic Intelligence

TruTYPE evaluates available genetic and non-genetic factors that may influence the patient's **current functional drug-processing environment**, including phenoconversion caused by interacting medications.

3. Evaluate Potential Exposure

The process identifies medications for which current pharmacokinetic conditions may be consistent with **increased or decreased exposure**.

4. Connect Exposure to the Known Risk

When the identified adverse effect or interaction is mechanistically related to drug concentration or exposure, the pharmacokinetic information provides an additional patient-specific factor for evaluating that risk.

5. Prioritize Personalized Medication Risk

TruRISK uses these combined factors to help differentiate established risks that may warrant greater clinical attention from those without the same patient-specific amplification.

Why Phenoconversion Matters

A patient's genetics do not change.

Their functional drug metabolism can.

A genetically predicted normal metabolizer can function differently when another medication strongly inhibits the same metabolic pathway. This phenomenon—**phenoconversion**—is recognized in pharmacogenomic literature and clinical guidelines.

That means a PGx result obtained years ago can remain genetically correct while no longer representing the patient's **current functional metabolic environment**.

Adding a medication can change that environment.

Removing a medication can change it again.

TruTYPE is designed to recognize this dynamic pharmacokinetic environment. TruRISK applies that information to medication risk.

The TruRISK Difference

Traditional medication-risk assessment can be thought of as:

Drug + Drug → Known Risk

TruRISK introduces another dimension:

**Drug + Drug + Patient's Current Pharmacokinetic Environment →
Personalized Risk Context**

And when additional pharmacodynamic and disease-related factors are incorporated:

**TruTYPE + Established Drug Risk + Pharmacodynamic Risk + Disease Risk →
TruRISK**

The objective is not to invent new drug interactions.

It is to better understand the **patient-specific relevance of risks that are already known.**

Supported by Established Pharmacology

The scientific foundation underlying TruRISK is supported by published research and regulatory guidance demonstrating that:

- Drug exposure is affected by metabolism and clearance.
- Drug-drug interactions can significantly alter systemic drug exposure.
- Genetic variation can alter metabolic capacity.
- Other medications can change genetically predicted metabolic phenotype through **phenoconversion**.

- Drug-drug-gene interactions can produce clinically meaningful changes in drug concentrations.
- Increased drug exposure can increase toxicity for medications and adverse effects with established exposure-response relationships.

These principles are supported by FDA clinical pharmacology guidance, CPIC pharmacogenomic guidelines, and peer-reviewed literature addressing phenoconversion and drug-drug-gene interactions.

A Dynamic View of Medication Risk

Medication risk is not necessarily static.

A patient's medication regimen changes.

Their functional metabolic environment can change.

Drug exposure can change.

And the clinical relevance of certain medication risks may change with it.

TruRISK

The Complete Picture of Personalized Medication Risk

Powered by TruTYPE Pharmacokinetic Intelligence

TruRISK is intended to provide evidence-informed medication-risk stratification and pharmacokinetic context. Inferred exposure is not equivalent to measured plasma drug concentration, and TruRISK should not be represented as predicting an absolute probability of an adverse event unless such predictions have been clinically validated.