Supplementary Tables

Table S1A. Comparison of Different Predictive Metrics for the most recent Chen et al. Data Set[13]

Criteria	% Correct (Positive Predictive Value, PPV)	% DILI Missing (False Negative Rate, FNR)	% Accuracy (ACC) (True Positive + True Negative)/192
Rule of Two	92.7%	58.9%	59.9%
Rule of Two + Reactive Metabolite Formation	100.0%	61.3%	60.4%
Dose ≥ 100mg+ 1 ≤ CLogP < 3	81.1%	75.8%	47.4%
Dose ≥ 100mg+ 1 ≤ CLogP < 3 + Reactive Metabolite Formation	92.3%	80.6%	46.9%
Dose ≥ 100mg	80.8%	15.3%	77.1%
CLogP ≥ 3	77.2%	50.8%	57.8%
Reactive Metabolite Formation	88.0%	16.9%	81.8%

Table S1B. Comparison of Different Predictive Metrics for the Chen et al. Data Set (Filtered for only BDDCS Classifiable Drugs)[13]

Criteria	% Correct (Positive Predictive Value, PPV)	% DILI Missing (False Negative Rate, FNR)	% Accuracy (ACC) (True Positive + True Negative)/166
Rule of Two	92.2%	58.0%	58.4%
Rule of Two + Reactive Metabolite Formation	100.0%	60.7%	59.0%
Dose ≥ 100mg+ 1 ≤ CLogP < 3	83.3%	77.7%	44.6%
Dose ≥ 100mg+ 1 ≤ CLogP < 3 + Reactive Metabolite Formation	90.9%	82.1%	43.4%
Dose ≥ 100mg	82.6%	15.2%	77.7%
CLogP ≥ 3	79.2%	49.1%	57.8%
Reactive Metabolite Formation	88.7%	16.1%	81.9%

Supplemental Figures

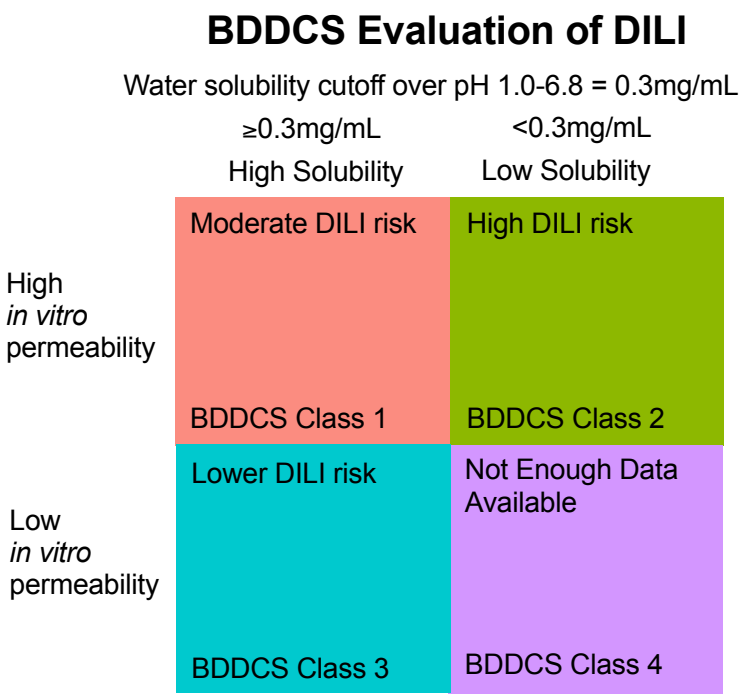

Figure S1. BDDCS Evaluation of DILI. Here we display the trends observed by using BDDCS to predict DILI potential. We suggest that the comparison of predictive metrics vs. just avoiding BDDCS Class 2 drugs may serve as a useful baseline in evaluating these metrics.

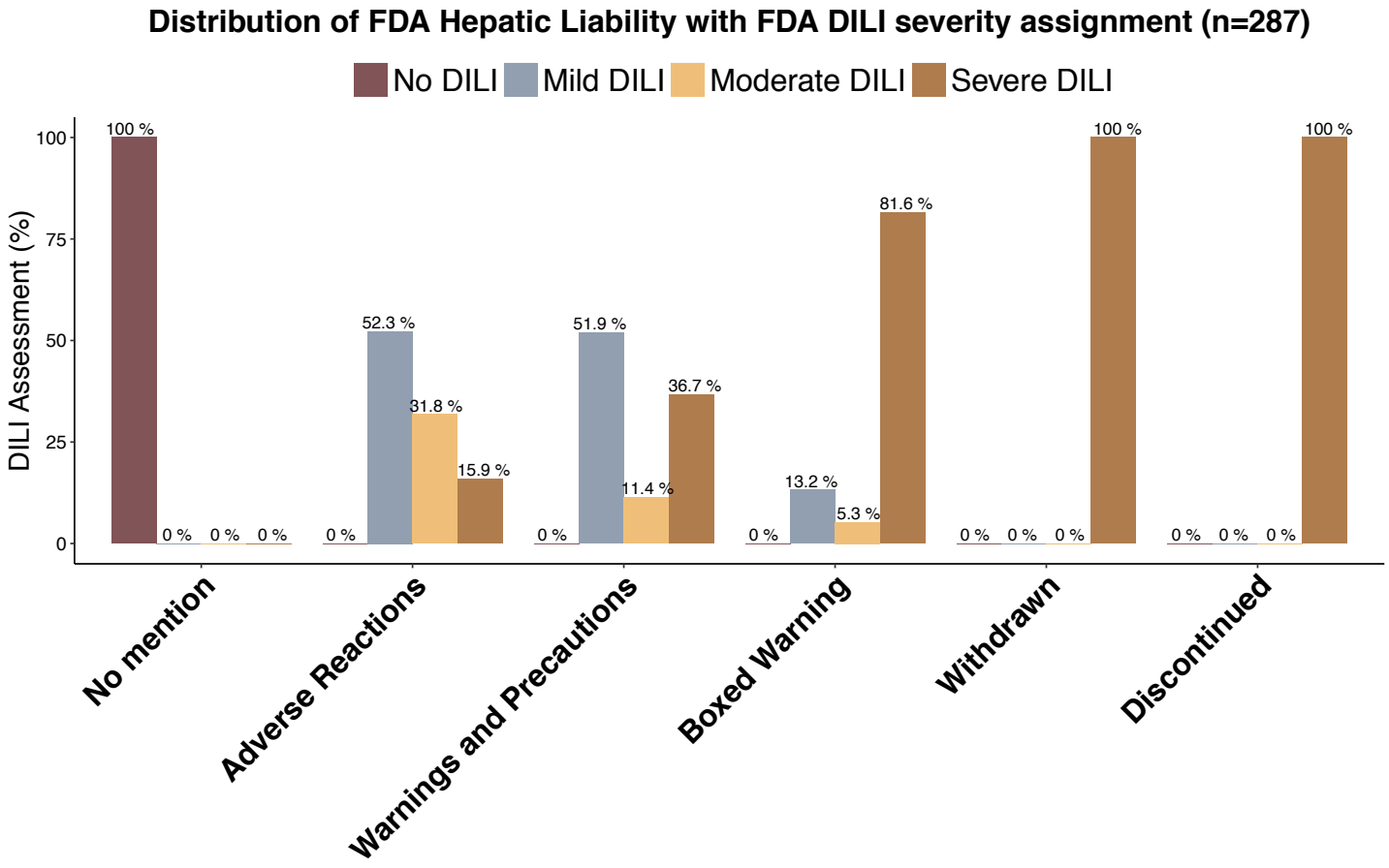

Figure S2. Confirming this classification, keywords that define severe DILI (e.g., acute liver failure and liver necrosis) were more often reported in the "Boxed Warning" or "Warnings and Precautions" sections than in the "Adverse Reactions" section. By contrast, milder DILI (e.g., increased liver aminotransferases and liver steatosis) were more frequently reported in the "Adverse Reactions" section. This indicates that classifying DILI severity according to the FDA drug label sections was applicable for the purpose of our study.

The "Black Box Warning" for moderate DILI was 5.3% (2/38) and 13.2% (5/38) for mild DILI. All of the discontinued (n=7) and withdrawn drugs (n=54) were labeled with severe DILI.

We note that under the FDA DILI severity assignment scale there are more compounds assigned to the "Moderate DILI" category in the "Adverse Reactions" section 31.8% (14/44) than the "Warning and Precautions " section (11.4%, 9/79).