

Supplementary Files

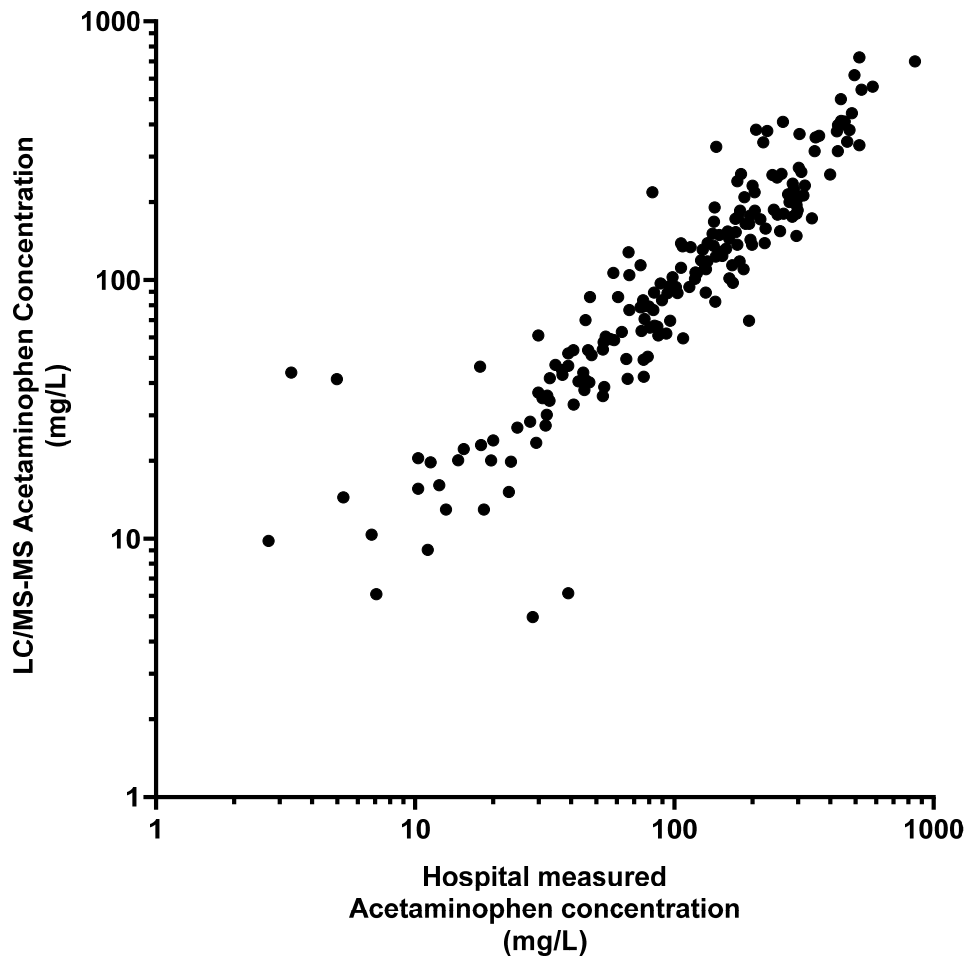


Figure S1: LCMS measured vs hospital measured acetaminophen concentrations (n=195).

Table S1: Outcome hepatotoxicity, only those patients with an ALT < 1000 U/L on presentation and not receiving acetylcysteine at the time of the initial acetaminophen and acetaminophen metabolite measurements

Metabolites/ Biomarker with initial acetaminophen concentration	No hepatotoxicity (median) (IQR, n)	Hepatotoxicity (median) (IQR, n)	p value	AUC ROC curve (95% CI)
APAP-hospital lab ($\mu\text{mol/L}$)	702 (301 - 1353, n=119)	1106 (453 - 1910, n = 21)	NS	0.59 (0.45 to 0.72)
ALT	20 (15 - 28, n=117)	133 (57 - 221, n= 21)	<0.0001	0.90 (0.81 to 0.98)
Acetaminophen Ratio	1.19 (0.43 - 2.01, n= 119)	3.45 (3.45 - 7.13, n=21)	<0.0001	0.82 (0.72 - 0.93)
Acetaminophen metabolite				
APAP-LC/MS ($\mu\text{mol/L}$)	646 (297 - 1145, n= 119)	867 (360 - 1460, n= 21)	NS	0.57 (0.43 to 0.71)
APAP-Glu ($\mu\text{mol/L}$)	461 (299 - 776, n=119)	568 (410 - 1120, n=21)	NS	0.61 (0.47 - 0.75)
APAP-Sul ($\mu\text{mol/L}$)	72.4 (50.4 - 102.5, n=119)	48.9 (24.7 - 72.2, n = 21)	0.0031	0.70 (0.58 to 0.82)
APAP-Cys ($\mu\text{mol/L}$)	9.4 (5.9 - 16.8, n=119)	37.1 (26.0 - 52.3, n=21)	<0.0001	0.87 (0.77 to 0.99)
APAP-Mer ($\mu\text{mol/L}$)	1.03 (0.61 - 1.74, n= 119)	2.26 (1.05 - 4.11, n= 21)	0.0023	0.71 (0.57 to 0.84)
CYP total	10.3 (6.8 - 18.3, n=119)	39.9 (27.8 - 55.3, n=21)	<0.0001	0.87 (0.76 to 0.98)
Total Metabolites ($\mu\text{mol/L}$)	545 (388 - 906, n=119)	654 (502 - 1237, n=21)	NS	0.60 (0.46 - 0.74)
% APAP-Glu	85 (79 - 89, n=119)	89 (82 - 91, n=21)	NS	0.61 (0.47 to 0.74)
% APAP-Sul	12.9 (8.5 - 18.2, n=119)	5.8 (4.6 - 9.9, n=21)	<0.0001	0.78 (0.66 to 0.91)
% CYP metabolites	1.64 (1.16 - 2.80, n= 119)	5.55 (4.09 - 7.89, n= 21)	<0.0001	0.85 (0.76 to 0.94)
Proposed Risk Stratification Tools				
APAP-Cys/APAP- Sul	0.12 (0.07 - 0.23, n = 119)	0.88 (0.63 - 1.08, n = 21)	<0.0001	0.91 (0.83 to 0.98)
ALT * APAP- Cys/APAP-Sul	2.65 (1.12 - 5.12, n=119)	134 (42.2 - 237, n = 21)	<0.0001	0.94 (0.88 to 1.00)
Acetaminophen Ratio*APAP-Cys	11.7 (2.33 - 22.5, n= 119)	110.1 (33.0 - 370, n= 21)	<0.0001	0.88 (0.79 - 0.97)
Acetaminophen Ratio*APAP- Cys*ALT	190 (58.0 - 525, n= 117)	16392 (1887 - 72202, n= 21)	<0.0001	0.95 (0.91 to 0.99)

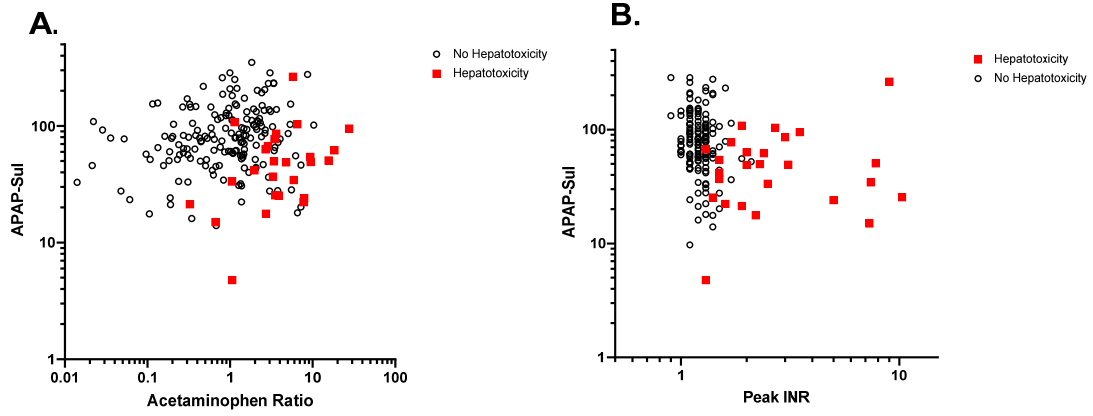


Figure S2: Correlation between A/ APAP-Sul and acetaminophen ratio (n= 200) B/ APAP-Sul and peak INR (n= 165)