

## Supplementary Appendix

### **Azithromycin and Major Adverse Kidney Events in Critically Ill Patients with Sepsis-Associated Acute Kidney Injury**

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**eTable 1. Sensitivity Analysis Using 50% Reduction in eGFR for MAKE definition**

<b>Variable</b>	<b>Odds Ratio (95% Confidence Interval)</b>	<b>p-value</b>
Azithromycin	0.52 (0.34-0.80)	0.003
Age (years)	1.01 (1.00-1.03)	0.077
Sex (male vs. female)	1.53 (1.09-2.15)	0.013
Baseline eGFR (ml/min/1.73 m <sup>2</sup> )	0.99 (0.98-1.00)	0.094
Diabetes	0.73 (0.50-1.05)	0.087
Hypertension	0.65 (0.44-0.97)	0.033
Heart failure	1.11 (0.76-1.63)	0.594
Liver disease	1.97 (1.37-2.83)	<0.001
Chronic kidney disease	1.86 (1.22-2.84)	0.004
KDIGO AKI stage (vs. stage 1)		
Stage 2	0.88 (0.58-1.32)	0.531
Stage 3	1.30 (0.87-1.94)	0.198
Lactate (mmol/l)	1.01 (0.97-1.05)	0.721
SOFA	1.14 (1.09-1.19)	<0.001
Anti-pseudomonal antibiotic coverage	0.72 (0.49-1.05)	0.090

eGFR=estimated glomerular filtration rate; KDIGO=Kidney Disease Improving Global Outcomes; SOFA=Sequential Organ Failure Assessment score

**eTable 2. Sensitivity Analysis Using Only Patients with Documented Baseline Serum Creatinine (n=345)**

<b>Variable</b>	<b>Odds Ratio (95% Confidence Interval)</b>	<b>p-value</b>
Azithromycin	0.79 (0.42-1.48)	0.463
Age (years)	1.00 (0.98-1.02)	0.939
Sex (male vs. female)	1.52 (0.94-2.45)	0.087
Baseline eGFR (ml/min/1.73 m <sup>2</sup> )	0.99 (0.98-1.00)	0.150
Diabetes	0.70 (0.43-1.16)	0.172
Hypertension	0.79 (0.44-1.43)	0.438
Heart failure	0.99 (0.58-1.69)	0.963
Liver disease	2.46 (1.47-4.11)	0.001
Chronic kidney disease	1.88 (1.01-3.51)	0.047
KDIGO AKI stage (vs. stage 1)		
Stage 2	0.61 (0.34-1.11)	0.107
Stage 3	0.84 (0.47-1.50)	0.546
Lactate (mmol/l)	1.06 (0.99-1.13)	0.094
SOFA	1.08 (1.02-1.15)	0.008
Anti-pseudomonal antibiotic coverage	0.72 (0.41-1.25)	0.239

eGFR=estimated glomerular filtration rate; KDIGO=Kidney Disease Improving Global Outcomes; SOFA=Sequential Organ Failure Assessment score

**eTable 3. Sensitivity Analysis for Composite Outcome of Death or KRT at Discharge**

<b>Variable</b>	<b>Odds Ratio (95% Confidence Interval)</b>	<b>p-value</b>
Azithromycin	0.59 (0.38-0.91)	0.018
Age (years)	1.03 (1.01-1.04)	0.001
Sex (male vs. female)	1.51 (1.06-2.15)	0.023
Baseline eGFR (ml/min/1.73 m <sup>2</sup> )	0.99 (0.98-1.00)	0.020
Diabetes	0.74 (0.50-1.08)	0.123
Hypertension	0.47 (0.31-0.71)	<0.001
Heart failure	1.00 (0.67-1.50)	0.982
Liver disease	2.04 (1.41-2.97)	<0.001
Chronic kidney disease	1.16 (0.75-1.80)	0.491
KDIGO AKI stage (vs. stage 1)		
Stage 2	0.91 (0.59-1.40)	0.661
Stage 3	0.93 (0.61-1.41)	0.734
Lactate (mmol/l)	1.02 (0.98-1.07)	0.263
SOFA	1.14 (1.09-1.19)	<0.001
Anti-pseudomonal antibiotic coverage	0.80 (0.54-1.19)	0.276

eGFR=estimated glomerular filtration rate; KDIGO=Kidney Disease Improving Global Outcomes; SOFA=Sequential Organ Failure Assessment score

**eTable 4. Sensitivity Analysis for Primary Outcome Using Only KDIGO Stage 2 and 3 AKI (n=422)**

<b>Variable</b>	<b>Odds Ratio (95% Confidence Interval)</b>	<b>p-value</b>
Azithromycin	0.64 (0.36-1.13)	0.126
Age (years)	1.01 (1.00-1.03)	0.120
Sex (male vs. female)	1.26 (0.83-1.90)	0.280
Baseline eGFR (ml/min/1.73 m <sup>2</sup> )	1.00 (0.99-1.01)	0.954
Diabetes	0.79 (0.50-1.24)	0.307
Hypertension	0.71 (0.43-1.15)	0.162
Heart failure	1.24 (0.75-2.06)	0.401
Liver disease	1.78 (1.12-2.83)	0.016
Chronic kidney disease	2.41 (1.40-4.14)	0.001
KDIGO AKI stage (stage 3 vs. stage 2)	1.40 (0.93-2.12)	0.107
Lactate (mmol/l)	1.02 (0.98-1.07)	0.344
SOFA	1.04 (0.99-1.10)	0.080
Anti-pseudomonal antibiotic coverage	0.78 (0.47-1.29)	0.328

eGFR=estimated glomerular filtration rate; KDIGO=Kidney Disease Improving Global Outcomes; SOFA=Sequential Organ Failure Assessment score

**eFigure 1. Range of Joint Relationships Capable of Explaining Away the Observed Effect of Azithromycin (E-value)**

