

## **Supplementary data**

### **Appendix 1 Forest plot for efficacy at each cutoff value (Figure S1-S10)**

#### **1.1 Forest plot for rate of treatment success at each cutoff value without control**

**(Figure S1-S3)**

#### **1.2 Forest plot for rate of treatment success at each cutoff value with control**

**(Figure S4)**

#### **1.3 Forest plot for rate of prophylaxis failure at each cutoff value without**

**control (Figure S5-S7)**

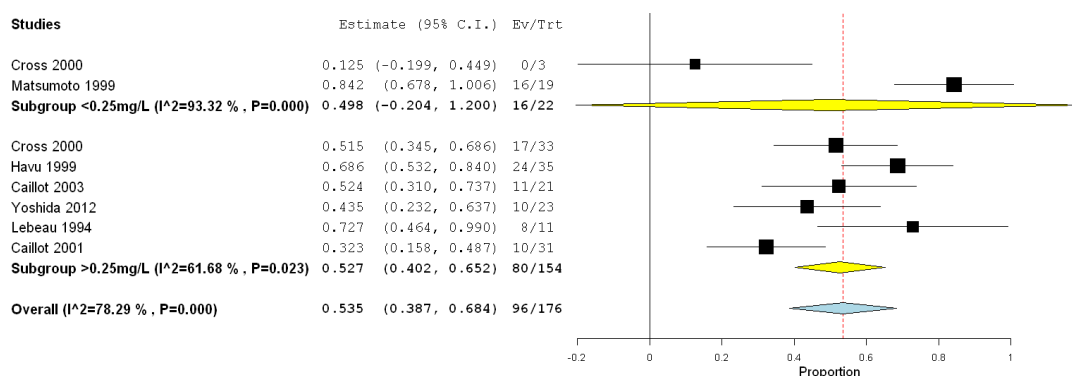
#### **1.4 Forest plot for rate of prophylaxis failure at each cutoff value with control**

**(Figure S8-S10)**

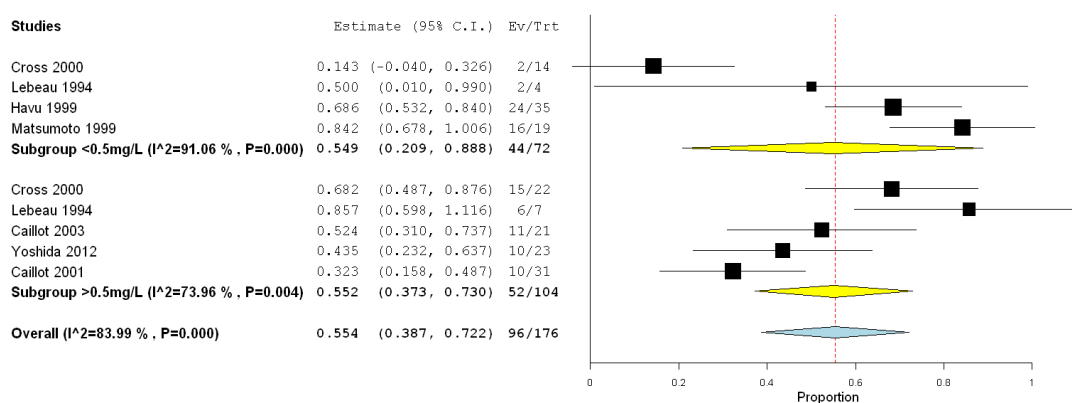
### **Appendix 2 Sensitivity analysis on each study's effect on the summary estimates for efficacy (Table S1-S2)**

## Appendix 1 Forest plot for efficacy at each cutoff value (Figure S1-S10)

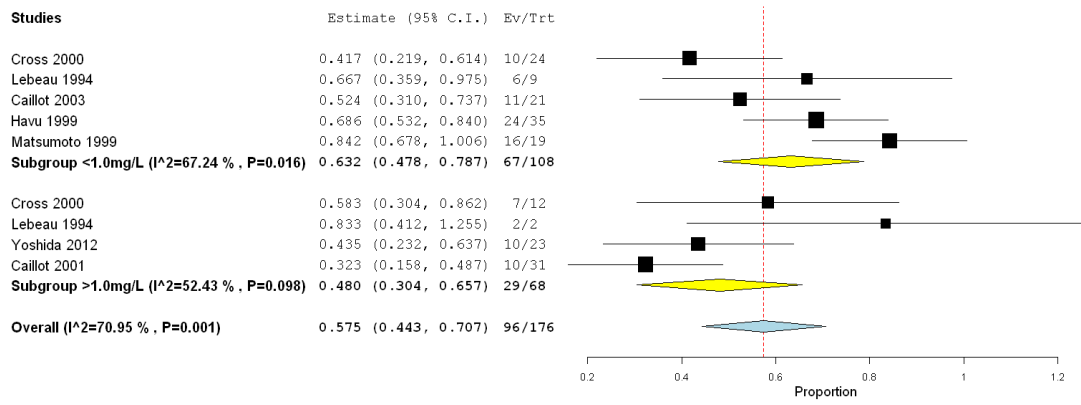
### Appendix 1.1 Forest plot for rate of treatment success at each cutoff value without control (Figure S1-S3)



**Figure S1 Meta-analysis for rate of treatment success (trough concentration of <0.25 mg/L comparison with ≥0.25 mg/L)**

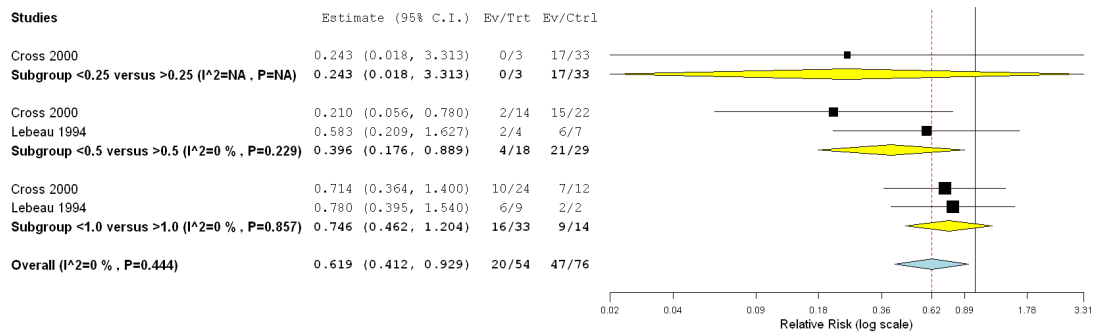


**Figure S2 Meta-analysis for rate of treatment success (trough concentration of <0.5 mg/L comparison with ≥0.5 mg/L)**



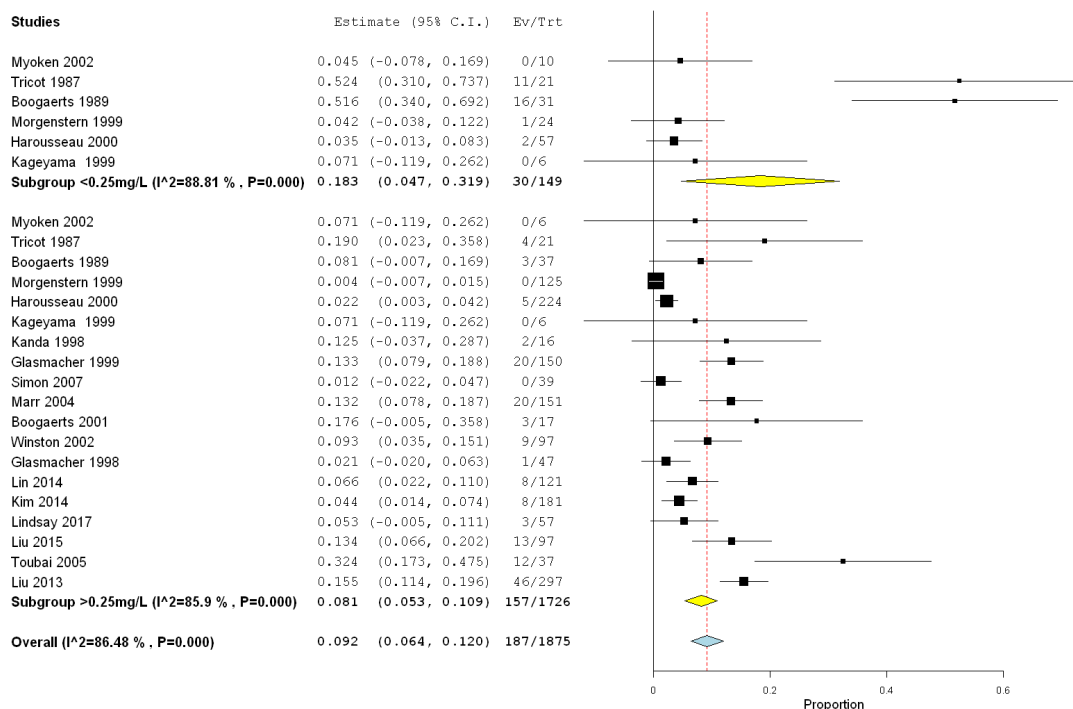
**Figure S3 Meta-analysis for rate of treatment success (trough concentration of <1.0 mg/L comparison with ≥1.0 mg/L)**

**Appendix 1.2 Forest plot for rate of treatment success at each cutoff value with control (Figure S4)**

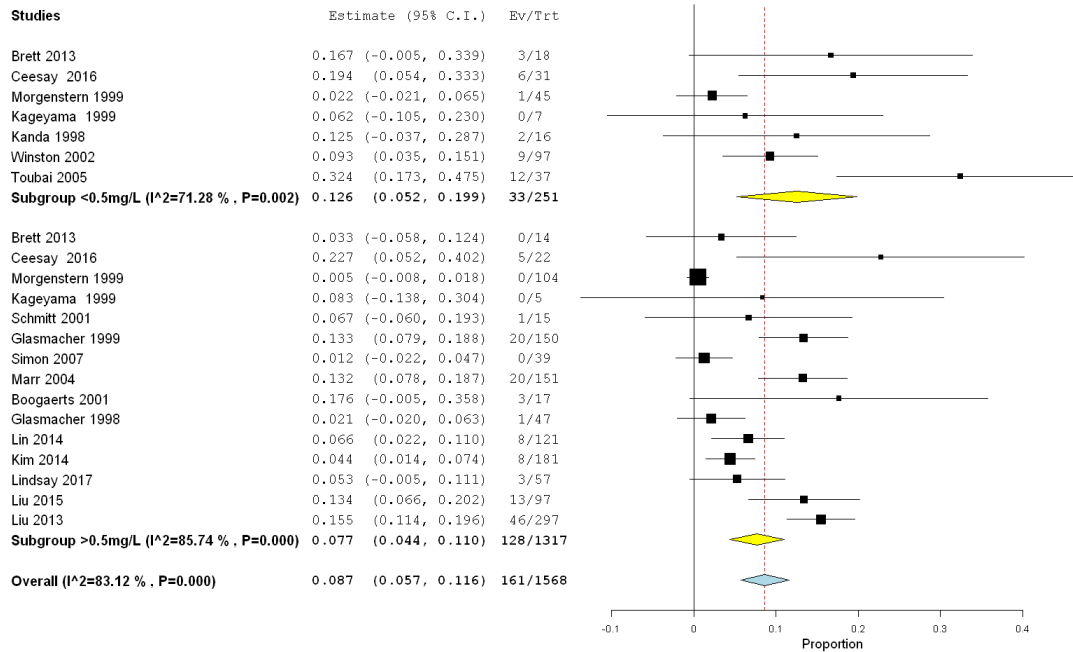


**Figure S4 Meta-analysis for rate of treatment success (trough concentration of <cut-off value comparison with  $\geq$ cut-off value, RR <1 favours  $C_{\text{trough}} \geq$ cut-off value)**

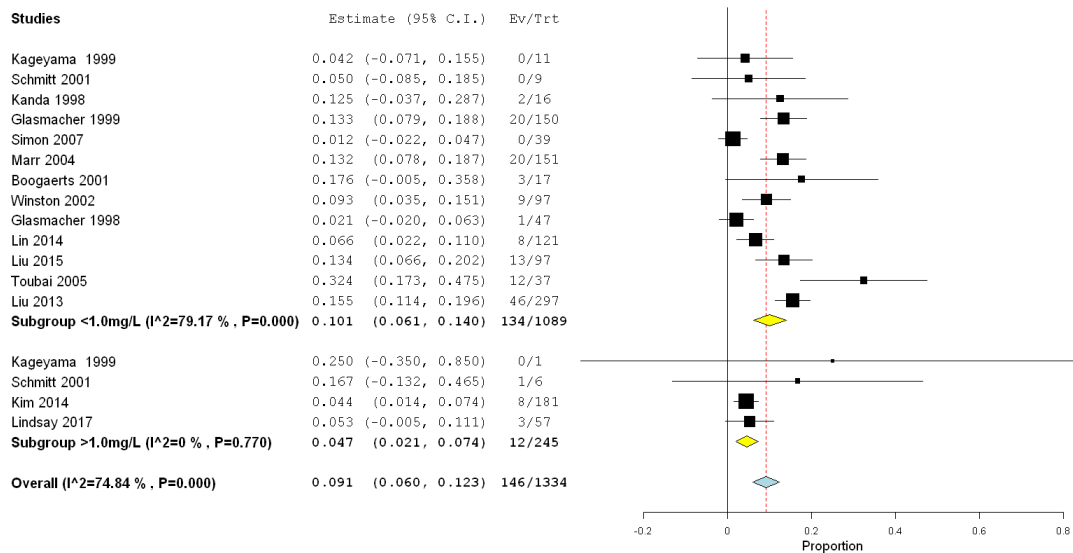
### Appendix 1.3 Forest plot for rate of prophylaxis failure at each cutoff value without control (Figure S5-S7)



**Figure S5 Meta-analysis for rate of prophylaxis failure (trough concentration of <0.25 mg/L comparison with  $\geq 0.25$  mg/L)**

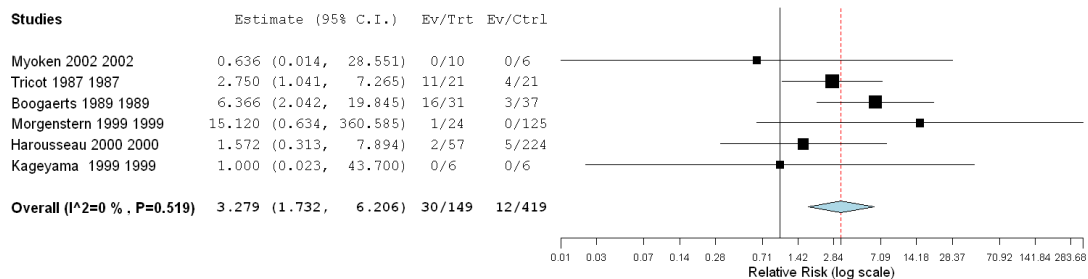


**Figure S6 Meta-analysis for rate of prophylaxis failure (trough concentration of <0.5 mg/L comparison with ≥0.5 mg/L)**

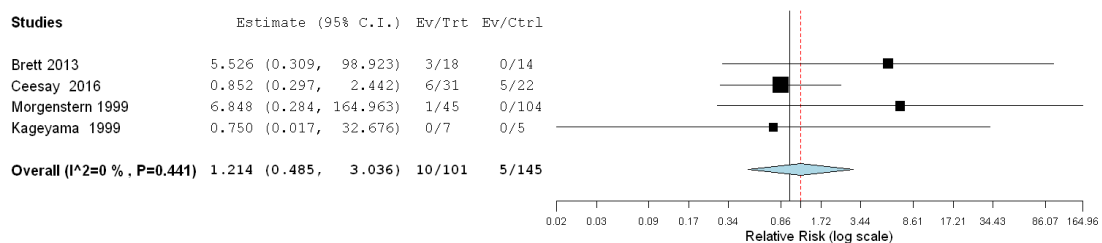


**Figure S7 Meta-analysis for rate of prophylaxis failure (trough concentration of <1.0 mg/L comparison with ≥1.0 mg/L)**

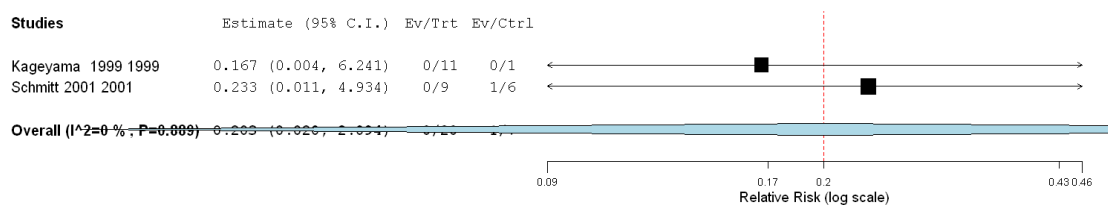
## Appendix 1.4 Forest plot for rate of prophylaxis failure at each cutoff value with control (Figure S8-S10)



**Figure S8 Meta-analysis for rate of prophylaxis failure (trough concentration of <0.25 mg/L comparison with ≥0.25 mg/L, RR <1 favours C<sub>trough</sub> <0.25 mg/L)**



**Figure S9 Meta-analysis for rate of prophylaxis failure (trough concentration of <0.5 mg/L comparison with ≥0.5 mg/L, RR <1 favours C<sub>trough</sub> <0.5 mg/L)**



**Figure S10 Meta-analysis for rate of prophylaxis failure (trough concentration of <1.0 mg/L comparison with ≥1.0 mg/L, RR <1 favours C<sub>trough</sub> <1.0 mg/L)**

**Appendix 2 Sensitivity analysis on each study's effect on the summary estimates for efficacy (Table S1-S2)**

**Table S1 Sensitivity analysis on each study's effect on the summary estimates for efficacy (results were only reported when differing from primary analysis)**

Cut off value	Rate of treatment success				Incidence of IFI			
	Sensitivity analysis	No. of studies attributing data for sensitivity analysis	Primary analysis	$I^2\%$	Sensitivity analysis	No. of studies attributing data for sensitivity analysis	Primary analysis	$I^2\%$
< 0.25	NA	1	0.498(-0.204, 1.200)	93.32	-	5	0.183(0.047, 0.319)	88.81
$\geq$ 0.25	<sup>a</sup>	5	0.527(0.402, 0.652)	61.68	-	18	0.081(0.053, 0.109)	85.9
< 0.5	-	3	0.549(0.209, 0.888)	91.06	<sup>c</sup>	6	0.126(0.052, 0.199)	71.28
$\geq$ 0.5	-	4	0.552(0.373, 0.730)	73.96	-	14	0.077(0.044, 0.110)	85.74
< 1.0	-	4	0.632(0.478, 0.787)	67.24	-	12	0.101(0.061, 0.140)	79.17
$\geq$ 1.0	<sup>b</sup>	3	0.480(0.304, 0.657)	52.43	NA	3	0.047(0.021, 0.074)	0
< 0.25 versus $\geq$ 0.25	NA	0	0.243(0.018, 3.313)	NA	NA	5	3.279(1.732, 6.206)	0
< 0.5 versus $\geq$ 0.5	NA	1	0.396(0.176, 0.889)	0	NA	3	1.214(0.485, 3.306)	0
< 1.0 versus $\geq$ 1.0	NA	1	0.746(0.462, 1.204)	0	NA	1	0.203(0.026, 2.034)	0

IFI=invasive fungal infection; -=no meaningful difference; NA=not application

<sup>abc</sup>,  $I^2$  decreased significantly after removing study



**Table S2. Summary of sensitivity analyses after removing studies**

Cut-off value (mg/L)	Remove study	RR (95% CI)	No. of studies	No. of participants in experimental group	No. of participants in control group	<i>I</i> <sup>2</sup> %	<i>P</i>
<b>Rate of treatment success</b>							
≥0.25 <sup>a</sup>	Caillot 2001	0.575(0.470,0.679)	5			31.13	0.214
≥1.0 <sup>b</sup>	Caillot 2001	0.556(0.358, 0.755)	3			32.79	0.226
<b>Incidence of IFI</b>							
<0.5 <sup>c</sup>	Toubai 2005	0.088(0.031, 0.145)	6			49.01	0.081