Co-amoxiclav

Records identified from PubMed & Ovid searches: 854

Records screened: 854 → Records excluded: 802

Full text articles assessed for eligibility: 52 → Records excluded: 29
No PK parameters: 15
Repeated data: 2
Participants <8: 5
Other: 9

Records included in analysis: 23

Piperacillin-tazobactam

Records identified from PubMed & Ovid searches: 661

Records screened: 661 → Records excluded: 509

Full text articles assessed for eligibility: 152 → Records excluded: 98
Participants <8: 47
Assumed PK parameters: 9
No patient characteristics: 5
Other: 37

Records included in analysis: 54

Meropenem

Records identified from PubMed & Ovid searches: 567

Records screened: 567 → Records excluded: 428

Full text articles assessed for eligibility: 139 → Records excluded: 86
Participants <8: 41
Assumed PK parameters: 16
No PK parameters: 16
Other: 13

Records included in analysis: 53

Figure 1 Flow diagram of studies identified in the review of antimicrobial pharmacokinetics
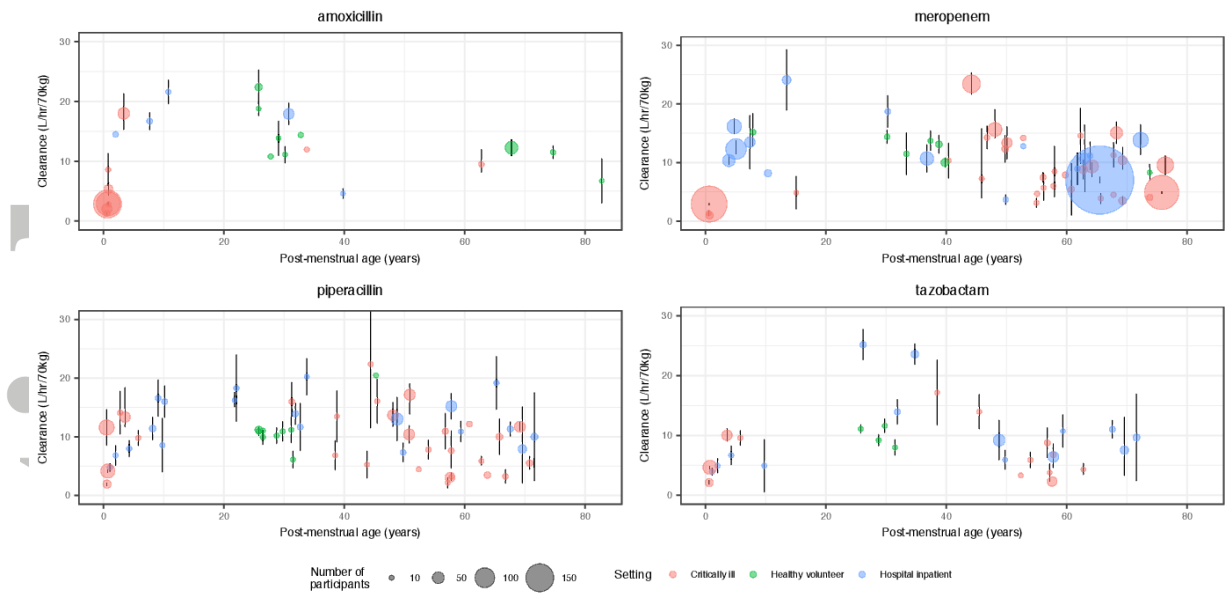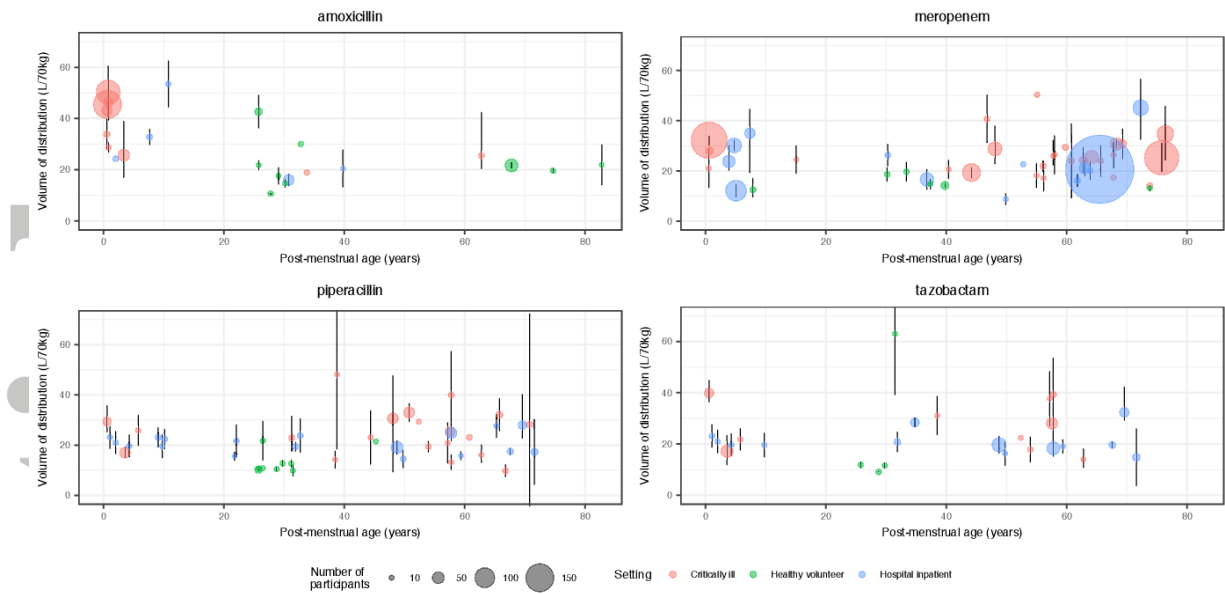
Figure 2 Weight-standardised clearance values identified from literature search plotted against age

Mean clearance values (standardised to a 70-kg individual) from each study are plotted with an associated confidence interval (where available). The size of the points is proportional to the number of participants. Colours are used to denote the setting of the study. There appears to be greater uncertainty in parameter estimates of studies in critically ill compared with healthy populations. As expected, there is a lower clearance in neonates and elderly populations, despite standardising values allometrically

Figure 3 Weight-standardised volume of distribution values identified from literature search plotted against age

Mean volume values (standardised to a 70-kg individual) from each study are plotted with an associated confidence interval (where available). The size of the points is proportional to the number of participants. Colours are used to denote the setting of the study. There appears to be greater uncertainty in parameter estimates of studies in critically ill compared with healthy populations. Weight-based allometric scaling appears to control for effects of age, except for amoxicillin where there appears to be a greater volume of distribution for neonates compared to adults.
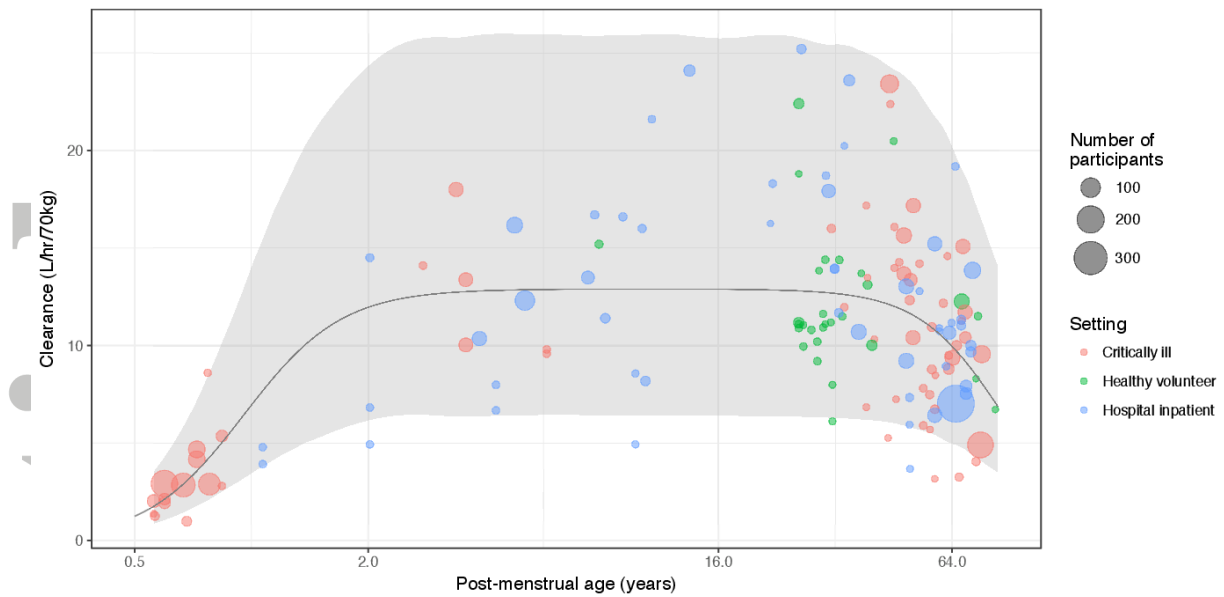
Figure 4 Visual predictive check of maturation-decline model for clearance using pooled data from amoxicillin, piperacillin, meropenem and tazobactam

The shaded area is the interval between the 2.5th and 97.5th centiles of clearance values simulated using the maturation-decline function (solid black line). Simulations from the model encapsulate literature clearance values (coloured dots) relatively well, although some sit below the lower confidence level
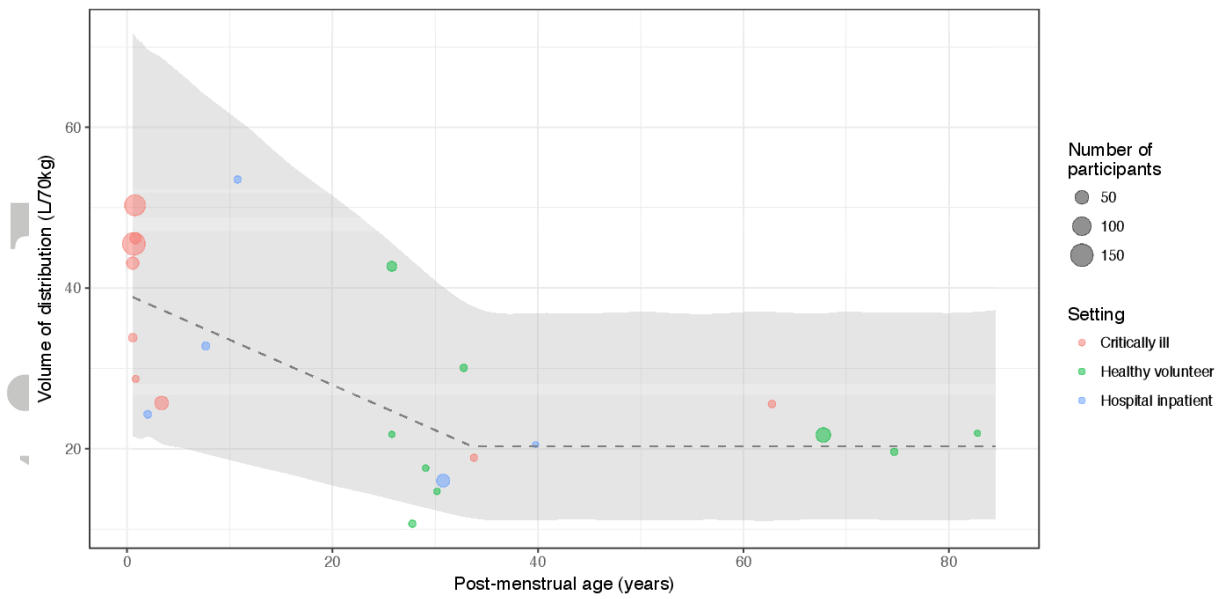
Figure 5 Visual predictive check of amoxicillin volume of distribution values using 'hockey-stick' function

Shaded area is the interval between 2.5th and 97.5th centiles of amoxicillin volume of distribution values simulated using hockey-stick function (dashed line)