Supporting information

1. Mean-variance relationship for quantitative PCR estimates of parasite densities

The key element of the random component in the statistical model is the mean-variance relationship (McCullagh 1983). To estimate this relationship for malaria parasite and gametocyte densities, we conducted additional experimental infections using the resistant clonal parasite lineage on mice that were independent of the experiments. Five replicate samples for asexual parasites in one mouse, and three replicate samples for gametocytes in two different mice were taken every two days during the infection. Due to the amount of blood necessary for conducting DNA and RNA extractions (see material and methods), these were the maximum number of replicates that could be taken from each mouse without influencing parasite kinetics.

The mean-variance relationship for both asexual and gametocyte densities is shown in Figure S1, and suggests a power relationship of the form $\sigma = a\,\mu^b$. This form of a variance to mean relationship indicates that the random component is a type of Tweedie distribution, which belongs to the exponential dispersion model family of distributions. The exact type of distribution is determined by the exponent in the power relationship. For asexuals, the power exponent is b = 1.59, which falls within the range of compound Poisson distributions. For gametocytes, the exponent is b = 2.206, which falls into a different class of distributions based on compound Gamma processes. Given that both values are close to a value of two, we assume that b = 2 for both and refit the a parameter. The assumed value of b=2 fits the data well (dashed line Figure S1), and simplifies the statistical model because it translates into an over-dispersed Gamma distribution. The power of this data is that we now independently estimate the dispersion parameter (a) without having to estimate it from the fitting procedure. The fit dispersion values are a = 0.01415 for asexuals and a = 0.0582 for gametocytes.

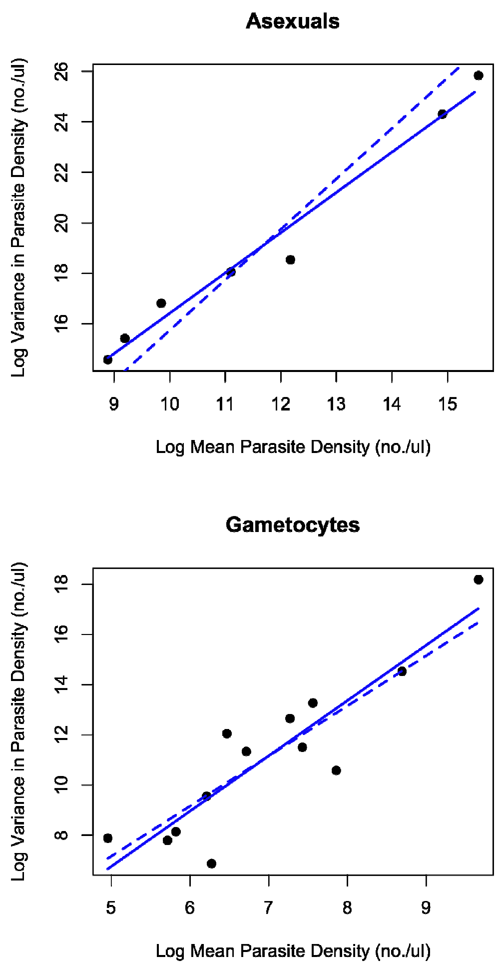

Figure S1. Variance (σ) to mean (μ) relationship for asexual and gametocyte malaria parasites. Points are raw data, solid blue line is the best fit assuming a power relationship $\sigma = a\,\mu^b$, and the dashed blue line is the fit assuming a slope of b=*2*. Parameter estimates for the dispersion parameter are a = 0.01415 for asexuals and a = 0.0582 for gametocytes assuming a fixed slope of b=*2*.

2. Examples of model fits to individual mice

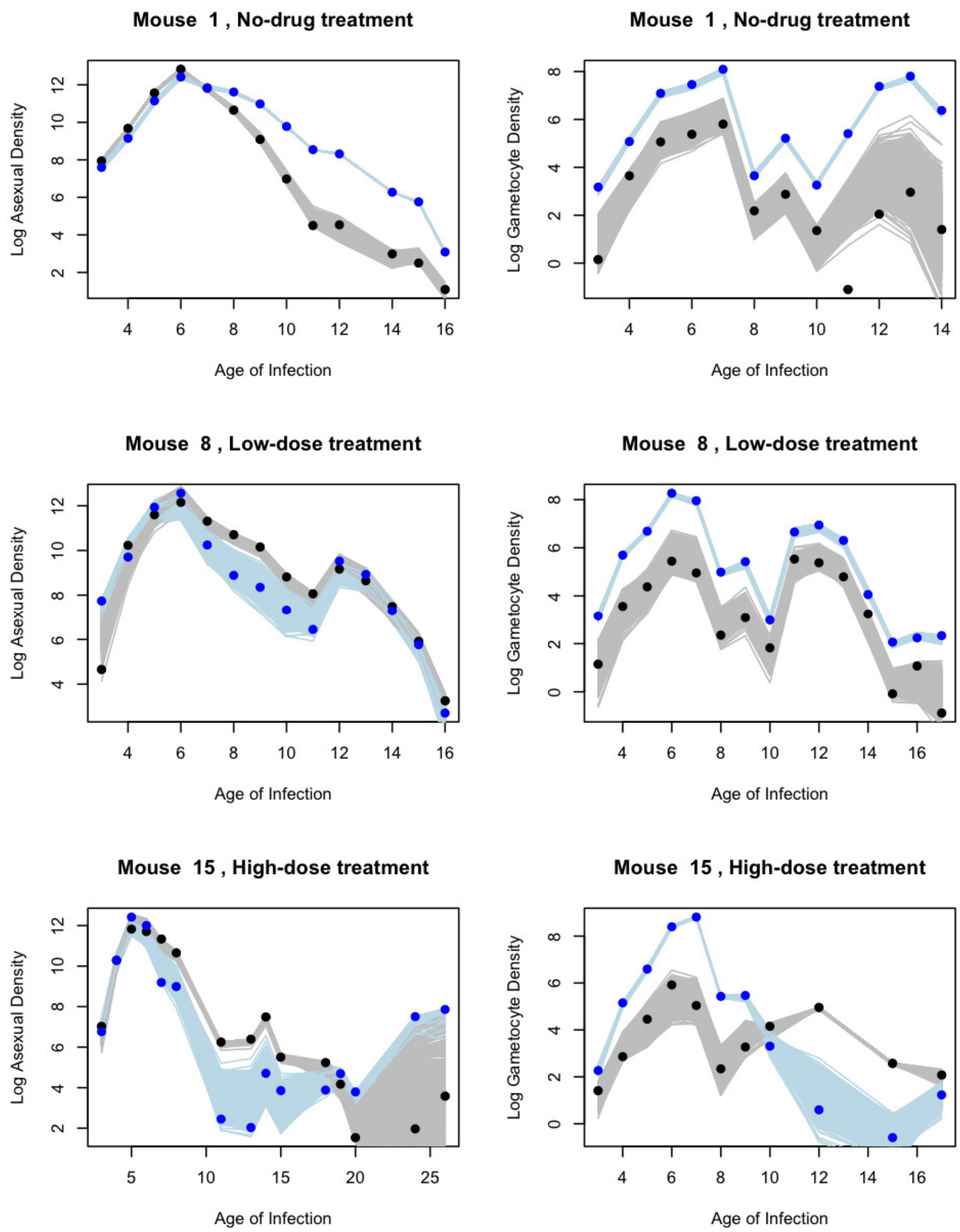

Figure S2. Model fits for asexual parasite densities (left panels) and gametocyte densities (right panels) on natural log scale for three arbitrarily chosen example mice that were either untreated (upper panels), received a low dose (middle panels) or a high dose (bottom panels) of pyrimethamine on day 6 post-infection. The blue lines represent bootstrap replicates (n=5000) of the parasite densities of clone R, the grey lines the parasite densities of clone S. The blue dots are observed values of clone R, black dots are observed values of clone S.