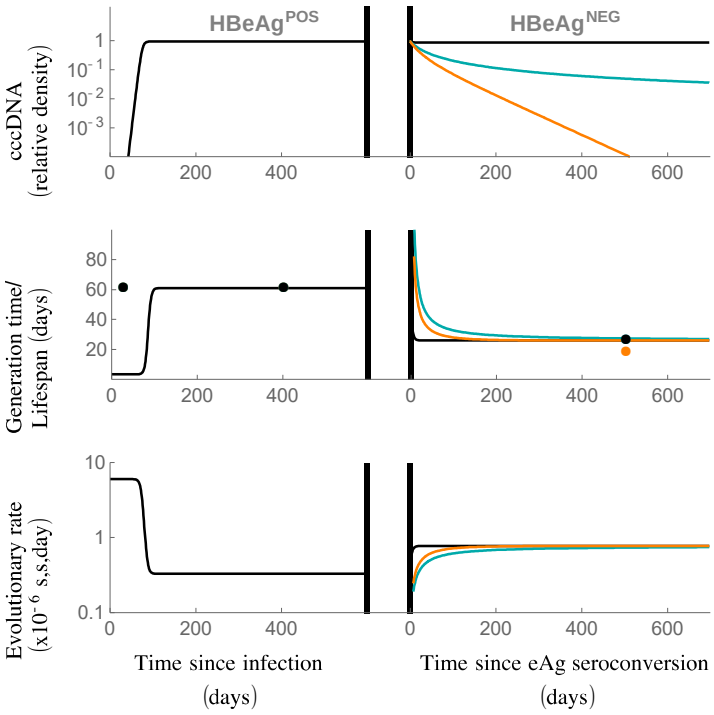
Estimating hepatitis B virus cccDNA persistence in chronic infection

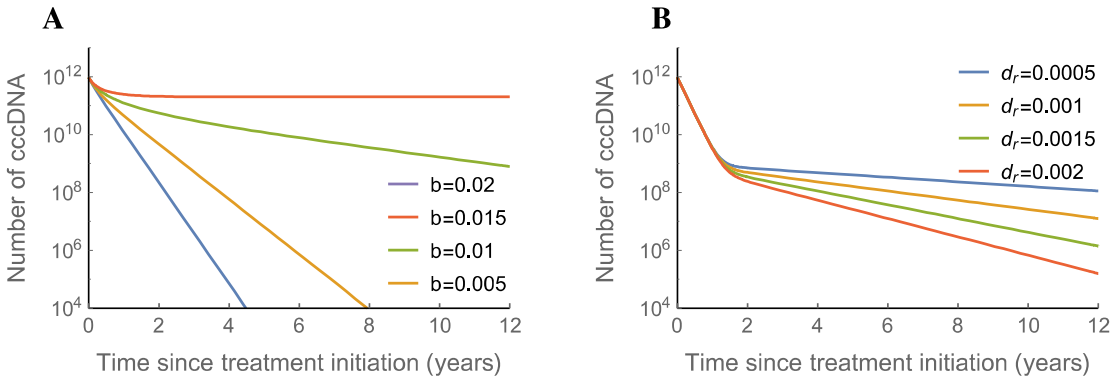
Katrina A. Lythgoe[1,2], Sheila F. Lumley[3,4], Lorenzo Pellis[5], Jane A. McKeating[6+] and Philippa C. Matthews[3,4,7+]

[+] Denotes equal contribution

Supplementary Figures



S1 Fig. Population and evolutionary dynamics of cccDNA for the within-host model assuming all cccDNA survives mitosis (q=1). The model was parameterised assuming the generation time, g, during chronic HBeAg^{POS} infection is 61 days, and during chronic HBeAg^{NEG} infection is 26 days, in line with our predictions for cccDNA generation time *in vivo*. The top panel shows the cccDNA burden, where 1 represents the maximum possible burden. The middle panel shows the viral generation time (lines) and cccDNA lifespan during key stages of infection (dots, derived from Eqs 9 and 10). The bottom row shows the evolutionary rates. Black line: replicative capacity during HBeAg^{NEG} infection remains the same as during HBeAg-postive infection (b_{eAg+}= b_{eAg-}=0.3 per day). Blue line: replicative capacity falls to b_{eAg-}=0.038 per day during HBeAg^{NEG} infection, and R_0=1. Orange line: replicative capacity falls to b_{eAg-}=0.038 per day and R_0=0.7. See Table 1 for all other parameters.



S2 Fig. Effect of NA treatment predicted by the model assuming all cccDNA survives mitosis (q=1). A: cccDNA dynamics whilst on treatment, assuming some residual reproduction. For all cells d=0.002 per day, δ=0.014 per day, c=0, q=1. B: cccDNA dynamics on treatment, assuming no residual reproduction (b=0) but 0.1% cccDNA is long-lived, for different death rates of long-lived cells, d_r per day. For normal cells d=0.002, δ=0.014, c=0, q=1, and for long-lived cells δr=0, c_r=0, q=0. The maximum number of cccDNA was assumed to be 10^{12}, and all model runs were started at equilibrium in the absence of treatment (b=0.3).