SUPPLEMENTARY FIGURES
Vera et al

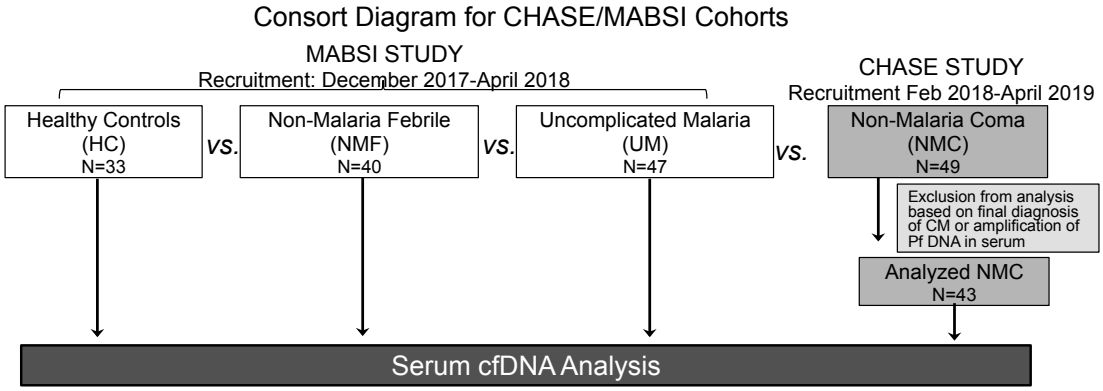

Fig S1. Diagram of cohort recruitment for CHASE/MABSI

Flow chart of patient recruitment for BMP study between 2017-2019. HC, UM, and NMF patients were recruited as part of the MABSI from Zingwangwa Health Centre in Blantyre, Malawi. HC subjects were recruited from Ndirande Health Centre attending for routine vaccine and health check up. NMC patients were recruited as part of the CHASE study within the QECH in Blantyre, Malawi. NMC patients were lost due to failure to meet inclusion requirements such as a final diagnosis of CM or positive detection of *P. falciparum* in samples by qPCR. Serum samples were collected and analyzed for cfDNA.

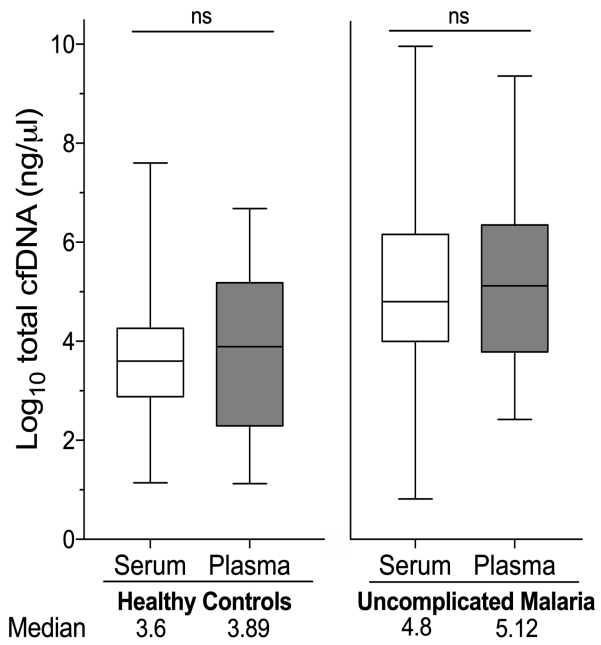

Fig S2. Comparison of plasma *vs*. serum total cfDNA measurements.

Total cfDNA measured using Qubit fluorometer for samples from healthy controls for serum (MABSI cohort, n=33) *vs*. plasma (BMP cohort, n=60) and from uncomplicated malaria cases for serum (MABSI cohort, n=47) *vs*. plasma (BMP cohort, n=77). Box-whisker plots denoting min-max ranges for total cfDNA concentrations. No significant differences in median levels were detected by Mann-Whitney test for single unpaired comparisons (plasma vs. serum).

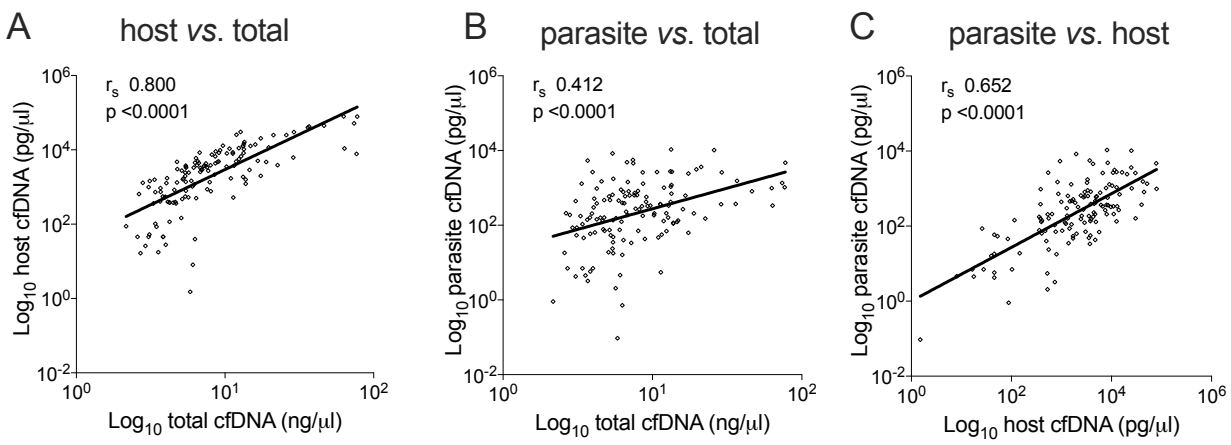

Fig S3. Correlations between the three cfDNA measurements: total, parasite, and host.
Spearman correlation scatter plots of CM samples for A) total cfDNA *vs.* host cfDNA (n=135), B) total cfDNA *vs*. parasite cfDNA (n=135), and C) parasite cfDNA *vs*. host cfDNA (n=135). Values were log transformed prior to plotting. Spearman coefficient (r_s) and p-value of correlation are denoted within graph. Solid line is a linear regression fit model of data.

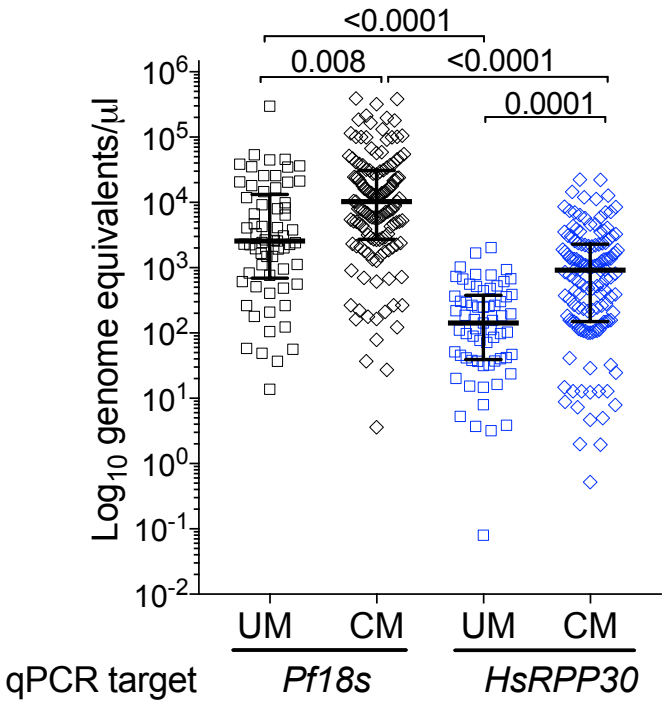

Fig S4. Parasite and host cfDNA expressed as genomic equivalents.

Levels of cfDNA in plasma samples from uncomplicated (UM, n=65) or cerebral malaria (CM, n=135) cases were quantified for either parasite PCR target (Pf18s, black data points) or host qPCR target (HsRPP30, blue data points), with calculations based as genomic equivalents (GE) from qPCR standard curves of known GE amounts, and graphed as scatter plots. Horizontal bar represents median with error bars representing interquartile range. Comparisons between clinical groups (UM *vs*. CM) for each gene target were determined by Mann-Whitney statistical test.

Table S1.	Malaria Patients	Non-Malaria Controls				Healthy Controls	
Clinical Parameters	UM (n=47)	NMF (n=40)	p-value[a]	NMC (n=43)	p-value[a]	HC (n=33)	p-value[a]
Age (months), median [IQR]	32.2 [19, 44]	21.3 [16, 42]	ns	64.4 [29, 118]	0.0002	14.1 [9.6, 25]	0.002
Male, n (%)	24 (49)	14 (41)	ns	22 (42.3)	ns	9 (30)	ns
Parasitemia (10^3/μL), median [IQR]	5.84 [1.5, 21.8]	n/a	—	n/a	—	n/a	—
Hgb (g/dL), median [IQR]	11.25 [9.9, 12.7]	11.4 [10.9, 12.1]	ns	10.121 [8.3,]	0.038	12.1 [10.3, 13]	ns
Hematocrit (%) median [IQR]	37.2 [33, 41]	35 [31, 39]	ns	31.3 [25, 35]	0.0002	39 [32, 40]	ns
Platelets (10^3/μL), median [IQR]	224 [141, 298]	206 [162, 326]	ns	288 [156-445]	0.045	257 [199-330	ns
Total WBC (10^3/μL), median [IQR]	8.29 [6.7, 10]	7 [5.6, 10]	ns	10.3 [6.8, 18.4]	ns	8.2 [6.8, 10]	ns
Blantyre coma score[b] (scale 0-5)	5 [5, 5]	5 [5, 5]	—	1[1,2]	—	5 [5, 5]	—

a. P-value between indicated group and UM, Wilcoxon rank-sum for continuous measures or chi-square test for categorical measures.

b. Blantyre Coma Score, scale 0-5; minimum score of 0 (poor consciousness), maximum score of 5 (fully responsive), score < 4 (abnormal response)

IQR, interquartile range; BCS = 5, no clinical coma by definition; n/a, not applicable; — analysis not determined.

NMF: non-malarial non-coma febrile, NMC: non-malarial coma