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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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APPENDIX MATERIAL

Emergence of artemisinin-resistant malaria on the western border of Thailand: a longitudinal study

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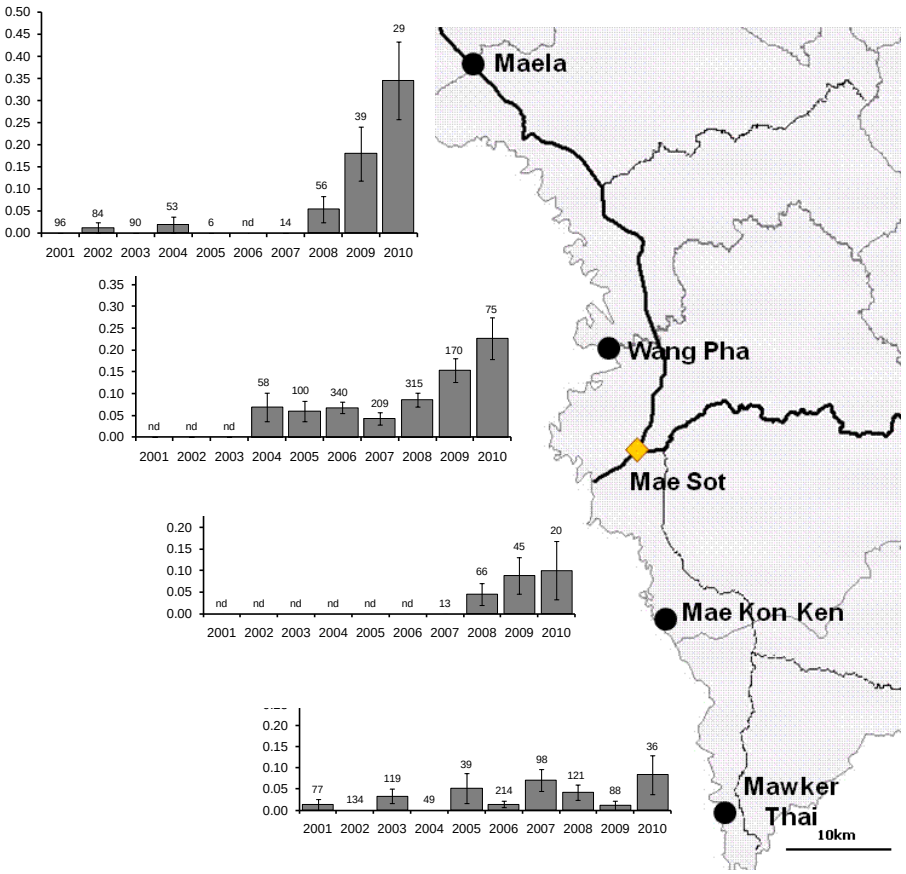


Appendix 1. Geographical variation in $t_{½}$ P. The section of the Thai-Myanmar border containing the four study clinics is shown, with bar charts showing changes in the proportions of slow clearing parasites ($t_{½}$ P ≥ 6.2 hrs) from 2001-10. Years in which no patients were treated are marked "nd". There is a sharp rise in proportions of slow clearing parasites in clinics north of Maesot between 2008-10.

Appendix 2: **SNPs genotyping**. SNPs are named by chromosome and position in genome version 6.2. Alternate bases at the SNP are shown in square brackets, with 50-60bp flanking sequence on either side.SNPs marked with an asterisk (*) are on the reverse DNA strand. These SNPs were chosen, because they are highly polymorphic in parasites from the Thai-Myanmar border, robust to genotype, and distributed accross all 14 chromosomes. These genome wide SNPs were used to accurately identify parasites that are identical (or very similar) over the whole genome, rather than because they are predicted to play a role in determining clearance rate. The SNPs are situated in coding regions in both synonymous and non-synonymous sites. SNP genotyping was carried out according to the Illumina BeadXpress instructions, using ~100ng template DNA. Excel version of table available on request.

Locus_Name	Sequence	Chr	Pos	Minor allele	Minor allele freq.
*MAL01-354427	TACTAGGTGGTTTATTTATATAAGAATTTGCTATGTATGTTATAACATCAGATTCATTTA[T/C]ATTATTATTTTGTTCTTCGTTTATGGTATTCTTTTTATTATTAGAAATATTATTATAATC	1	354427	A	0.43
MAL01-539149	TCTCTTTTCAGTGGATGCCATTTGTTTTTTTAAATGTGTTAAATCATTGTGAATTTTTAT[A/G]ACTTTAATAAATGTACGCATAAAATCTTTATATTCATTATTTTTAAAATATTTCTTTACT	1	539149	G	0.31
MAL02-217337	TTTGTTTAGAGCATCATTTATTTTTGGAAAACATCCCTCCTTCAAAGGATCATACGATTC[A/T]TTTCCTTTCATACAAAAAAATAAAAAAAATTAAATAAATAAATATACACATATATATAAA	2	217337	T	0.29
MAL02-322398	TTACACATAACAGAAAAAACATTCATTTGAACCCTTCAGTTTGGTTAAACAATATCCAGG[A/G]GATGTTTTATCTTTACATTCATTCCAATGGAGTTCACAAAATTTAATACATCCTTCATGT	2	322398	G	0.26
*MAL02-660994	TTTTTAAATAATATGTCCAAATGTGTTTTATACCAAAAAAAAGAAGCATATCAAGAATCA[T/C]CAGAACAAAACTTCCATGGTCTTATAAATCATAAAAATGAAGACAATGAAAAATGTCATA	2	660994	G	0.17
*MAL03-249686	ATACAAAATAAAGAAGAGGAAATTATAAAATATGTTAATGAACTACAAAA[T/C]AGTGATGTGCAAAAAGAAAAAAAAGAGTTGAAAACAATAAATGAAGTTTT	3	249686	G	0.49
MAL03-439621	AATTTATTATTTAATTATTATAACAAAGAAAGTATTGGACATAAAAAAAA[A/G]AAAGCGAGTTTTGTAAAAGCACAATATGCTAATAATAGGATACCATCTAA	3	439621	G	0.25
*MAL03-704420	ATTAATGTGTTTTTAATATTTGAACAATATTTTTCAAACATTTCATTTGC[T/C]CGTGTTAATGTTATGATTTTCATTTGAGCTTTATTTAATAAATCGTTTAA	3	704420	G	0.17
MAL03-748204	CAATATGATAGAACTGTAAGAAATTCATATGGAGATATTATTCAATTTTT[A/G]TATGGAGAAGATGGTATGGCAGGTGAATATATAGAAGATCAAATTATAGA	3	748204	A	0.44
MAL03-822470	AAATATGGTAAATATAAAAATAATAATAATAACTCTTTTATAACATGAGAGATGAT[A/G]CAGAATTGACAGACATTGAAGAAAATATATCAAGTAAAAAAAAAAAAAACAAATTTATAG	3	822470	A	0.39
*MAL04-268436	TCTCATATTTATTATTCCTATTCATAAGTAATAAACCTTTGTTGTATTTTCGAAACACAT[T/C]TTTATGTCTCCTAAGATATACCACATTTTGGACATTATTATTATTATCATTATTATCATT	4	268436	A	0.29
MAL04-307321	GATGATCATATATGGAATTATAATTTAATGGGAATCAAATTTAATAATAATCAAAAATAT[A/G]CACCACATCTTGATATACCACAACCATTTTATGCAGATATACATAGACCAAATCACTTTC	4	307321	A	0.16
MAL04-393114	ATTGATAACCACCAAGGTAACGAAACATTTCAACATGAATAATATTGAAAGTAAGAACAAT[A/C]TTGATGGTATTCGTAATATGAACCATTTCAAGAGTGTGATTCCTTCAGATATGACAACAA	4	393114	A	0.45
MAL04-443828	CTTGCTATAACTATTAGATTTTGAGATGAAATTATTGATAAGTTCTTTAA[A/G]GAACCCACAGCACTTATTAAGCGTGCCGTTAATGAACTACCTAATAACAT	4	443828	G	0.28
MAL04-469608	CCATGATTTTCGGCAACGGGCGTGACCCTACTGCCGCTTTCGCCTATATC[A/G]ACTACAAGGGCTTTTGAAAAACAAGATAAAAAGGAAATATATAAATGAAT	4	469608	G	0.44
MAL04-494108	AAATAAAATTATAAACATGTCTACAAACATAAATGGAGCAATCGAAAGGTCAAATGTTTC[A/T]ACATACAAAAACAATCATAATAATATGTTATGTAGTAAGTTGGTGCATCAGGTTCCTTCC	4	494108	T	0.35
*MAL04-809686	ATATCAAAACATAACAAGTTATATCTTCAGTATGATCAAAATAAAAGAAACTCTGAAATA[A/G]AACATACAAATCACAAAGAAGATTATTCGATGTGCGACAATGTGATAACAAGCAAAATGA	4	809686	nd	nd
*MAL04-933828	GGATAACTCTAAATATGTGGAATGTGGGAATGGAGACAAAGAAACGAATGATTATAATAC[T/G]CGTCGAAAAAAGAAGGATGAGAAATTTAGTGTTAGTAGTAATGCTTTATATGATATGAGT	4	933828	C	0.35
MAL04-994352	ATTTCCTTCATTTTTATTAATATCAAACATATTATTTAAATGATTGGATTTTTATTTTCTTTATATTTTCATTAATTTCCTCATTACGTTCCTCAATTTCAATAACATTTTCTTCTTTT	4	994352	T	0.42
MAL04-1037032	CTTAAGTAAATTTTTAATAGATAAGAAAATATCTAGTGAAATATTATTATCGGAAAAAGA[A/G]CATGTAATAAATGAAGAATTAAAAGAGATTTTACCATTTGGATTTGGAATTCATCATGCA	4	1037032	A	0.44
MAL04-1101563	AATTTTTTAATTTTAATTCAAGTGGATATCATAGTTGTATGAGAAAAGAATTTTCGAATC[A/C]TGCATATAAATGTTTTGCAGGGAAAGGTTTTTCAAGTATGTTTAATCTGGACAAAAAAAA	4	1101563	C	0.29
MAL04-1140617	GATAAAAATTATTCAAGGAATATATTAAATAATGAGAATTCTGAAGATATATTTGAATCG[A/G]TTAAAAGGGTAGAATCGTATAATTATGAAAATAATATGGTCAATGAATGTAATGTAATCC	4	1140617	G	0.46
MAL05-118209	CTTCTCTTTTCTTAACCATATTAACATAGAAATTCATATTCCTTAGTTTAACTTTTTTAT[A/G]TTTTGTTCCCTTCCATTTTTCTCTTTTGCAATTTTTCAATGATTTTTCTTTTATATGCTT	5	118209	G	0.28
*MAL05-385372	AAAAAATTATTCGATGATCTAAAAGATCTTGAAGAACTTTTTGGTGATAG[T/C]GATGAATTAAAAGAATTAGAACATGAATATGATCATATTAATATAAACGA	5	385372	A	0.11
MAL05-720978	TTATCTTCTGTATCATATATATAAAAATAATTTTGCTCATCTAAAACCCA[A/G]AGTCTATTTTTTCGATCAAAGGCTAGAGATTTTAACTTAAAAATACCATA	5	720978	A	0.31
*MAL06-154776	TCCAACACATCCTTTTTTTTCTCATGTTCAATATTTTCTTTACGATGTACTGCGGACATA[T/C]TAAATCGTTTAATATTTTTCCTTTTAACATTCTCATCATAATTATTCAACACATTAGCAC	6	154776	A	0.30
MAL06-410691	ATACATGTATAATAAAAAATGTTGTGGTCATCTTCAACTAAAAAATGTTGAAGAATTGTC[A/G]AAGTTTGATTGTTTATTAATAAATATGGGAATAAAATTTCGAATTATTTATATATTTAAA	6	410691	A	0.27
*MAL06-573730	AGAAAAACGCTCAAGGAAATTTTACACTCAGCTTAGATGATGAAGCCATC[T/C]TATCCTCTTATAATAATCCAGAAAAGAATAATACTGTATGCAAAAATAAT	6	573730	A	0.20
*MAL06-593821	TCATTCTTTAATTCTTTTATTTTTCTCAAAACATTGTGCATACTCTTAAA[T/C]CCATAAGATAAGATTACCCTAAACACACAATTATTATTATTAAATAAAGA	6	593821	A	0.22
MAL06-937750	ATAGGTTCTCCAATACCTATAGGAGGATTTTGTATAATGCATGTAGCAAT[A/G]CCCCCAACACTATCTCCTTTATTTTTTAGTTTCAAAATATAAGAACAAAT	6	937750	A	0.39
MAL06-1184507	AAAAAAAAAAAACGCAAATTAATAGTGATAATTATGTGTTGACTATCAAAAATTTGATCG[A/G]TGAAAATATAGAGAACAAATCTGTAGAAAAAAAAAGGAAAAGAAATTATTTCAAGAAATA	6	1184507	G	0.46
MAL06-1206499	CGTAGTGAAAGTGAAATAGATGATATAGATGAATTAGATGAAGAAGAATATGATTGGACG[A/G]AGCATGTATATAATTATAAGCCTACCACTTATTTATTACCTGGGTTGGGAGGAAGTACAT	6	1206499	A	0.12
MAL07-476303	CATGTCGGCACACGGAGGAAGATCCCCCTCAAACATTTTTGCTCCTTCCATGTTTTTCAT[C/G]TGCCCTGTTGAAATATCCATTTTTTCATTAATTTCCTCCTGAGAGGTTATATAATTACTA	7	476303	G	0.30
MAL07-511352	GTTTATATTTGTATTAATTTTAATTTATTTACTTACCATTTTGATTGAAAATGATATGTA[A/G]GGCAAATTAAATTTCAACTTATTCATGTTTACAAAAAATAAGACAGGTATATATGAAAAG	7	511352	A	0.42
*MAL07-543849	TTTTATTTTTTTTTTTCTCCATATCTATTGTAGAATCATTTTTATAATTATCTAACGCAT[T/C]TGTTTTTTTATCATAACTGGAATCTTTATTCATTTCATTTTTGTCATTTTGTAACAAGGT	7	543849	G	0.31
*MAL07-672051	CATTTTACTTAATGTTCATATGTATAATTTTTCAAACGAAAATGGGACAATAAAATATAC[A/C]CCGATAGATGGATATAATATTCCTGTTCCTAAAGAAGAAAACGATATGAATAATATGGTA	7	672051	nd	nd
MAL07-759749	AAGTATCGAAAGAAGGATTAAGGAGAAACACAGAAATATAGAAGATGAAGACTCAGAGGA[A/G]AGTGACAGCAAATGGAGGAGAAGAAAAAGGGAACGAAGCAGAGATAAATATAAAGAAAGA	7	759749	G	0.33
MAL07-1122023	ATGATATATTATTTTATTGTATTAATTATATCATTATGTTTAAAGGAAAGGAAATATTTT[A/G]AATTGTTGAAAAAAAAGATAAAAATGGATATTATACAATGGCTTCATTATGGTTTTGTAA	7	1122023	A	0.44
*MAL07-1289206	TTTAATAACTTGTTTTTTTTTATTATTGAATTGTGCTTTTTCTACATGAATTATGCAATT[T/C]TGTCTAAAGAGAAAATTATCAAAATATTTGATGGCCATGTCTACACTTTGTGTATATACA	7	1289206	G	0.15
*MAL07-1311707	TTAATAAATAATAATTTTAAACATGATGGAGTTGGTAATATAAATATGTATGATGGAAGG[T/C]TTAATAAAAATGAAGAGCAAAATTATTTACCACACCCTTGATGGAACATAAAAATATAA	7	1311707	A	0.08
MAL07-1323949	GGTTGATGAAGCCATGAATAAAAATAAAATTGTTTTAGATTCATTAGAAAAAATGAAAAC[A/C]TGTGAAGTATGTTTGATTGTAATGAACTAAAATCGTTAATTGAAATTATTCAGAAAAAG	7	1323949	A	0.31
MAL08-417613	AAAAGATAAACTGCCTAATAAATATGCATGGTTTCTTTCGGATGGTACATCGATTTGCAT[A/G]TAGGCAGGCATACATACATCATCGTTTAAAATCATATATTCTTCTGGATGTAATTCAATG	8	417613	G	0.41
MAL08-477431	AAATATAAATGTACCACAAACACATGATAAACAAAAGTGTAAGGAAAATTTTTCAAATTC[A/T]TTTGTTAATGAAATATATGAAAAAGAAGAAAAAGAAACGCAAAAAATGAAAGAATATTTA	8	477431	T	0.43
*MAL08-502163	TTTAATTTTTACACCTATGCTCTTCCTTATATATTGAGTTAAAATTTCCGTTTTCTTTAC[T/C]TCGCAAGAATATACTTGTGAAGCATTAAATATACAAAAAGGAATAGATTCATCACTTATT	8	502163	G	0.12
MAL08-1057901	AAGAATCTTTCTATTATGGGTTTGTGTAAAGAGAAAATAGTGTTAACAGAAAAGGCAACA[A/C]TATTTAATAACATTGAATTGTTGTATTCATATTATCTTATAGTTCAGAACGAAGCTTTAG	8	1057901	C	0.34
MAL08-1101130	CATGAACACAATTTAAAAAAAATATTAGTACCCAGACATTGCATACCGCC[A/G]CAGGATTATCAAAATGAAGAATTGATAGCAAAAGATGGACAAATTAATAA	8	1101130	G	0.21
MAL08-1292195	ATTTTGAGATTTCTGTAATTATATTATCAAGGTCTATCATAGTAGAAGAAGGAGAGGGGT[A/G]GTCTATGTTAGTTGATCTTGTTAAATCAGAATTATTTTTGGATATATTAGGTCCAAATTAGGTTCTGTTTATG	8	1292195	G	0.39
MAL08-1311981	AAATCTACTCCTGAAATACTTAAAAAAGTATGGGAAAGTGATATAGATAAAAATTTACCA[C/G]GCTTGATGGAGAAAACAACCAAAAATACTTGTGTTAGAGTTGCACATGATTATGAAAAGG	8	1311981	C	0.37
*MAL09-492618	TATATATAACACTATTCAAAATTGTCCAATTGATTATAGAAAGGAATTGCTAAGAAATAT[T/C]TATCTTACAGGAGGTTCGAGTATTATAAGAGGCTTTAGACAAAGATTGGAGAATGAACTC	9	492618	G	0.24
*MAL09-631767	AGATCTTTCTTTATGACCAATGCATATGATTTAACAACCGTCTTTTCTTTATCAACAGTT[T/C]TGTCTTTTTACCATCTCCACTTTTGGATATATTAGTGTCAAATTAGGTTCTGTTTATG	9	631767	A	0.22
MAL09-692487	ATTTTTATTATTACTATTAATATTCTTGTAATTGTTGAAATGTGTTATATTGGGCATACA[A/C]ACATTTTTATAATTTTCCGAAGTCTTTACATTAACTTTTTCTATAACAAAATTCCACGGC	9	692487	C	0.28
MAL09-771381	AAACGACACAAATGCTAAATGCTTTTGTTCCTTTTGATTTGGATCCTCCACCTTTGTATG[A/C]TGAAAATCCTGAAACAGTTAGGTAAAATATTATATCCAAAATGGAATAAATACACCCATA	9	771381	A	0.50
*MAL09-1111191	ATCAAAAAAAAACATTAGTAACATAATAAATAATAATGTAATATTAAATAACTGTTCAAA[T/C]AAGGTGTCTAATAATGATTTCGATGATGAAAAGGACGCATATTTACAACATGAGTGGAAT	9	1111191	G	0.44
*MAL10-113266	ATGTACATATTTTATTTTATTTTATTTTACATTGTTGTCATTCTTTTTCTTTTTTGCAG[T/C]ACATTTTTAAGAGGACACGAATAAAAATCATCGAATCATTAAATAATGATAACAATGTAG	10	113266	A	0.48
MAL10-317580	AAGGATGATGATTCTATAATAGATTTATTAACTGTTAATGAAAATTCTAT[A/T]GATGCCCCAACACAAGATAATGAAAATAAAATTAATAGTTTACAAGCATT	10	317580	T	0.37
MAL10-336274	AACCATATGACACCTAAGATGAATTTTAATATTATGGAATATCTAATGTCTGATAATTAT[A/G]TTCATATTAATTCTCCTCAAAGTTGTTTTAATACATTAACCATAAAAAATGAATTACATG	10	336274	A	0.46
MAL10-404541	AGATATGACCCTATGGGCCCTTTTGGTAACGAGCCAAATTCTGACAATAG[A/G]CCGTTTGAATATCAAAATAATTTCCCCTTTTAAAATTTTTTATTCTAATT	10	404541	G	0.49
MAL10-631275	TGGCTTAGATCAATCATATTTTCATTTACTTGTACTTCTTCCTTTTCTTTAAATAAATAA[A/T]CATCATCAGGTAGGAGGAAATTATCATCATAATTAAATTCATTAGGAGTATATGCTTTTT	10	631275	T	0.22
*MAL10-663198	TACTATAACCACTATAATCCGTAGTATTAGAATTATGATGTCGTAAATCATCTGTGCCTT[T/G]AGTAGTACCACATGCCATTTCATCTACACCTACATTTTGATATTCTACAAAATGATCATT	10	663198	A	0.26
MAL10-1300115	TAAAAAATGTAATAATCATAATAAATATAGAAAGATCGATGAAAATGTAAAAGGTATACA[A/T]CTTGTTGATGGTTCAAAAAAAAATATACAAAATGATGAATATACATGTGATGATAACCAA	10	1300115	T	0.19
*MAL10-1385891	TAATAATATAACCGTTAATGCAATCATTCCACATGTACGTAAAGAAATTTACATTTCC[T/C]ATAGAAGAAAGAATTCCAACAGGAACTTTAATTCAAGAAAAAATTATAAAACACTTGTT	10	1385891	A	0.30
MAL11-185094	GTATATCCATTTGTGGATTATAATCCGAATCAAATAAAATAACAATATCAGCAGTCGTTA[A/G]GTTAATACCAATACCACCAGCTCTGGTAGATAATAAGAAAATAAAATATTTACTATTCGG	11	185094	A	0.43
MAL11-255830	CCATAAATAATTCATCTGCTTGTTCTATATGTTTAATATCAATAATTGTGTTACCTTCTA[A/G]GGTAGCTAAAATTCTGGATGGTTCTAATAATAACATAGCAAATCTTAGAGATGACTGTAT	11	255830	G	0.47
*MAL11-281726	ATTATGTAATTCTTTTTTAACTTTAGATTTTATACCTATACGAACAACATTCTTAATATT[T/C]AAATCTTCAACACATTTTCTTAAGATATTATCAACACTTACATTGCTAGGACCTGTTACT	11	281726	A	0.37
*MAL11-304323	TTATAATAGTGTGCATTATTTTCCTTTTCTTTAATACTTGCCTTGCTACT[T/C]CTTTTCTTATCCTCATCTTCATTTCTTTTTTTCATATTTTCATTATTTAC	11	304323	G	0.14
*MAL11-683964	AATAGCTAGTTCAATTTCATACGCATCAACAGGTAATTTCCCTGTATATTGCAAAACATC[T/C]TTTTGTGTGTGCAAAAATAAACCAGCATTTACGTCTAGTACAATTTTGCCATCAAAAATA	11	683964	G	0.40
MAL11-769993	CCATGTGAATATAATATTGTCTGTTTATTTAAATCCAAAGGTTTCTTATATAACATTATA[A/C]CAGATACTTCCGTCGAACCTCTTTTTAGTTTTTTATAATTTATATCGATATTATTTATCT	11	769993	A	0.15
MAL11-896199	CTATTGGTATCATTCACACTGTTTGTATAATTCACATTATTTCCATCCAC[A/G]TTTTTGAGATTCATATTTGTTGAATCAGTAGGATCTTTTATTATAGTACT	11	896199	A	0.23
MAL11-1331758	TTTTTTATGAAGCAAAAAAAAAATAAATCTAAATCAAATATGAAACAAGATGATTATTAT[A/G]CCGATTCGGATCAAGAAGAAAATGTACAAATGAATACCGATGGAAAAATTATTATTCGTT	11	1331758	A	0.39
MAL11-1520975	CAAAAAAATGAAAATTTACTAAACGAAAACAATATGGATAATATAAACATGCAGGAAAAA[A/T]GTGAGACGGAAGAAGATTTAGATTTAGAAAGAGATGAAGATAAACATGATGCTCCACCTG	11	1520975	A	0.29
MAL11-1749804	ACAGCTCCTGAATAAACTTCACTACCTCCTATAACACAAATTTTACCTGA[A/G]CACCCTTTATATTCATCTTTGCGGAGTTTCGGAACAATCACATCCTTGAT	11	1749804	A	0.39
MAL11-1802198	TTCTAGTACCTGTTCAGATAACTTTGGGAATCGATTTAATACTCTGTTGGCTATTTTTTG[A/G]GATAAAATTCTAGTGTCTGACTTACTCTATCTAGACAATTAAAAACAGGTGCATTAATT	11	1802198	A	0.32
*MAL12-83177	TCTTTTTTCATTTCCTTGTTTATTTGAATATTCATCGTCATCATCATCTTTTTTTAAATA[T/C]AAATGCATAATAGCGTTTTTAAAATCTGCCTCTCTTATATGTTTCATTTTCTCTATATCG	12	83177	G	0.15
*MAL12-114173	TACTTATGGAAAAATAGAAAAAGACTTTGCTTTGATTAATGCTAGATTGGAGACCCTACA[T/C]ATAAAAAAATCATTCAGGTTTTTAAAATGATAATCCATATATATAAATGAATAAGTATAT	12	114173	A	0.18
*MAL12-262199	TATATGAATTATATTTTATTTATTTATTTCTTTTTAAGGATTTGGATAA[A/G]CCGGAAAGAACTTTACAAGATACCGAAATTGTTAGACCTCAAAACAAACT	12	262199	nd	nd
*MAL12-529412	TTCCCTCAAGTTCATCATTGTATCCATCAGACGTTTTATTATCCTTTGGCCTACACCATC[T/C]ATTTTCATCAAGTGTTAAATCACCACTACAACCATCTTGCATTCTTAATCTTAATTCTGG	12	529412	A	0.29
*MAL12-1116275	ATATGTTATTTTCTATTTTTTGTGTGTCCTTTTTTGTGTTTGCACTATCTTGATTAATAT[T/C]TCTAATGTCCGTTGTGCACGTGGATGAATAAGATTGTTGAAATTTTCTTTTTTTTTTTATT	12	1116275	G	0.48
MAL12-1131597	CTTTTTCATGTCTATAATATTTTCTTCATCATTTATTTTATCATTTGTGGTCGAATTATC[A/G]TTTTTATATTTTCCAAATCTTCACCATATACATATTTTTTGGATATATTACTATCCTCG	12	1131597	G	0.34
*MAL12-1156125	AACAATATGAGTAGTTCAAAGAGACATATACCACATGACATGAACCCAGA[T/C]GATAATATTGAGAAATATTTTTCAAATCTTTGTAGTGGTATAGAGGTAAT	12	1156125	A	0.35
*MAL12-1591944	GACTACAAGCATTTTATCATAAAATAAATCACCCAGCTATATCGCCATTT[T/C]TAATAGGATTATTTCCTACAAATAATGCACAAAATATAAGATTCTGTATT	12	1591944	G	0.37
*MAL12-1761553	ACTATTTATATTATTATATTATCATTACTATTATTGTTTATCGCATTTTCAGGATATCC[T/C]ATCCAGTTGGTGCTATTATTTCCTTCATCACATTTATCAACATAATCATCCTTAACATAC	12	1761553	G	0.29
MAL12-2046727	TTCCAATTTATATGTATTATTTTTTAATTGATAAAAATGACCATCTTTATGATTTGTTAT[A/G]TCTAATAAGGAATGAGAATGTTGCAAAAATTTTATTATTAATTTTTTAGTAACATCTATA	12	2046727	G	0.47
MAL13-146947	TTATTTTATTGGTATTACTCAACCAAGAAAAATAGCTGTAAAAAGTATTTGTAATAGATT[A/G]AACGATGAACTAAATGAAGAAATATGTGGTTATCAAATTAGGTTTGAAAAATCGTATTTT	13	146947	G	0.39
*MAL13-210569	TAATAATTATTACATATCATCTTTTTTTTATTATCGGTATAAAATTCAGTATTTTCTTTT[T/C]CCTTTATCTTATTCTTTCTTTTCTCCTGCCCCTTACTATTATTTGATATTCTTCTTAACC	13	210569	A	0.29
MAL13-619422	TTTTTTCAGAGCCTGCAACTTTCCACGTGAACCTACCCTAATATTTACCA[A/G]TCCTTTTTTATTAATATTATAAAGGGTATGTGATATATTCTTGTAATAAT	13	619422	A	0.46
*MAL13-1233419	TTTACATAATTTTCGACGTCATCATTTTCATTATTACTCATAATTGAATTATCCACAATG[T/C]TTGCCTCTTTTACAGCTTTACAAAGTTGGTAAAAAATATGATAATTCCTTTCACCTTCTT	13	1233419	A	0.34
MAL13-1966774	CGTGTCACATTTTATTAAACCTAAATCAATTAACTGTTCAGGTTTTTTTA[A/G]TATACCACTTTCTTCATGTAATTCTTTTACAGCATTTTGTAAAAAGTCTT	13	1966774	A	0.29

MAL13-2158308	TTATTTTTGTTTGAATATATATTCAACTTCTTTGATGCATGTTCTGAAATTTTTAAGTAA[A/T]CTTTTTTTTTTTTATTCATGTCATTTTTCTTGTCCAGTTCGTTCATATATTGATTTTGCA	13	2158308	A	0.26
MAL13-2570163	TATTAAATTAAAAGAATTTTTTGAGTTCAAAAAAAAGTATTCATCTAAATTATGATTTTC[A/C]ATTATTGATTTAAAACATTGATCAGAAGCAGTTCTTAGAGAAATTAAATATTCATTATCT	13	2570163	A	0.46
*MAL14-990875	AGTAGTGCTCATAACAACATGCATCATAATATAAATCATCAAGAAAATTA[T/C]AGAAATCAAAACAGCTATAGCCACTTTTCTGGTCATGGTAGCTATATCGA	14	990875	G	0.32
MAL14-1199184	TACAGTATATACTTTAATATCTGTACCAAAGGTAGATAAAAATTCTTCATATATATATGT[A/T]CCATTAGTTCGAACTTTATGTATTTCTGGACAATATTCACTACTCCTATCCTTAATTTTA	14	1199184	A	0.38
MAL14-1458321	TAGTTGAATATGCTGAAGAGGTAGAATTAAAGAAGAAGGTTGAAAAAACATTTATGGGAG[A/G]AAAAGTTAATATGACAGAGAATCGCAGTGTTTTACATACAGCTTTAAGAATACCCATAGA	14	1458321	G	0.45
MAL14-1757546	AGAGGTACATATTAATAGATTTTTTAAATGAAAATAGTAATAAAAATAATGTAACGCATG[A/G]TGATAGTGTATTACCAAATGGTAATGAAACGGACGCGAAAAAAAATGTGGATGAGAATAA	14	1757546	A	0.32
MAL14-1853537	ATATGCTCGTATATCATTCAAAATATTAAGATGCATGATTATATCTGTAATAAGATGAGT[A/G]ACATTTATAAATACACAATTCAATTTTTTTAACATTTCAACAGGACTATTATTCAGGTAT	14	1853537	A	0.36
MAL14-3017684	ACACATCCAGAGGAGAGTATTTCATCTTGAATAAGTCATCCGTTAAAACATTCTGAAGAG[A/T]AGATCTATCTTTCTTCTTATCCAATAAAACATTTTTCTCTCGGTTCATATCATGAAGCGG	14	3017684	T	0.37
MAL14-3124926	TGTGAAGAAGAAAAAGAATTAATGGGAGCAGCTGGAGGAAGATATGTCGAAGAAGAGGTA[C/G]AGGGAGCAGTTGGAGGAAGAAATGTGGATGAAGAGGTAGAGGGAGCAGTTGGAGGAAGAA	14	3124926	C	0.34

Appendix 3. Age structure of patient population

Age category (yrs)	Frequency	Percent
<5	666	20.8
5-15	1109	34.63
≥15	1427	44.57
Total	3202	100

Appendix 4. Multiple regression analysis of t1/2P, stratified by location. Locations (from North to South) are Maela (MLA), Wang Pha (WPA), Mae Khon Ken (MKK) and Mawker Thai (MKT). The influence of patient age, prior malaria exposure, gender and sampling date on log t1/2P were examined using least squares regression in (A) all samples and (B) only patients with clearance data showing a good fit to a linear model ($r^2 \geq 0.8$). In both analyses sampling date strongly influences t1/2P in three of the four locations (black shading, white text). Significance of associations with patient age, gender and malaria exposure do not fall below p=0.025 and fail to reach Bonferroni corrected table-wide significance levels (0.05/16=0.003) in both analyses.

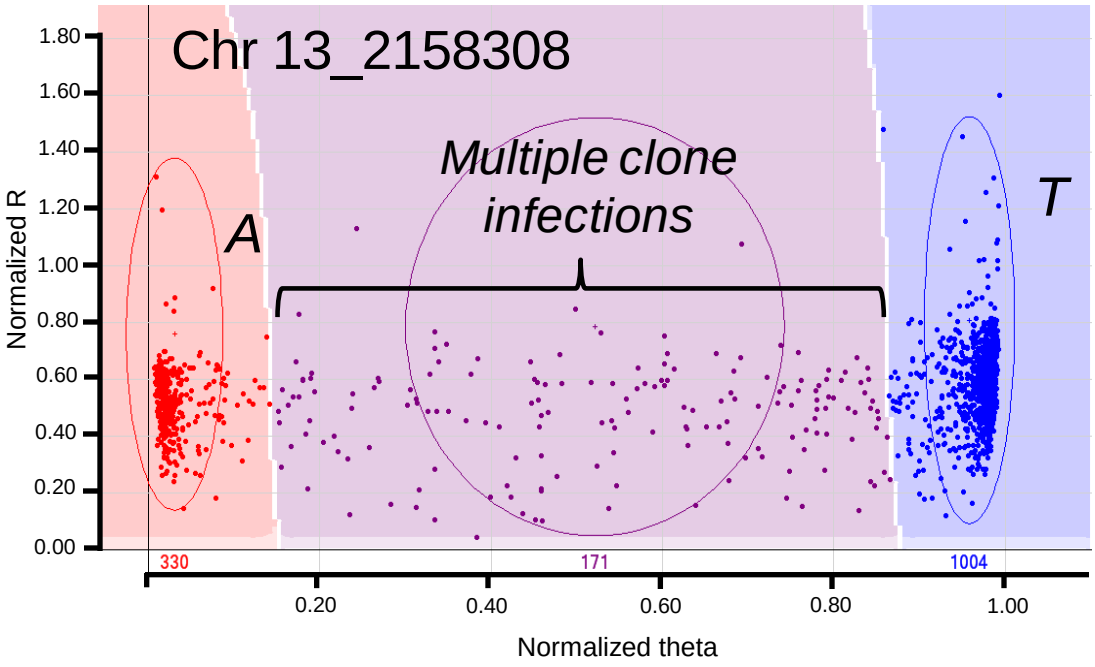
(A) t1/2P measures calculated from slopes with r^2>0.8 only

	MLA	n=433	WPA	n=1244	MKK	n=141	MKT	n=931
	F	p	F	p	F	p	F	p
Admission Date	82.834	8.9E-20	12.678	3.7E-04	0.943	0.332	14.123	1.7E-04
Age (yrs)	1.440	0.230	2.686	0.101	0.232	0.630	0.005	0.944
Malaria exposure[1]	0.016	0.899	2.457	0.117	0.287	0.592	4.512	0.034
Gender	3.301	0.069	0.639	0.424	1.827	0.176	0.748	0.387

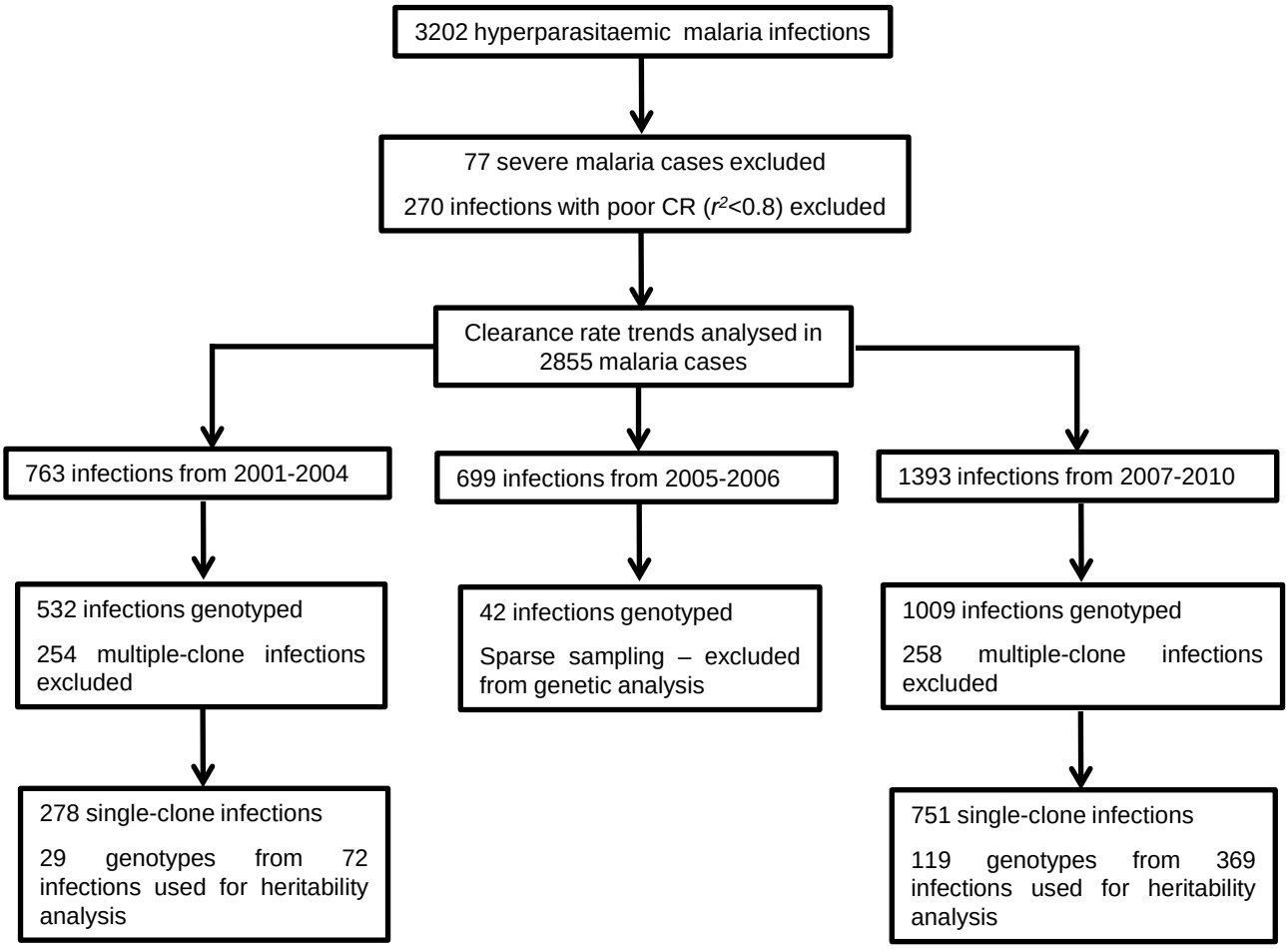
(B) All data

	MLA	n=444	WPA	n=1346	MKK	n=150	MKT	n=1038
	F	p	F	p	F	p	F	p
Admission Date	79.154	5.7E-19	13.430	2.5E-04	0.292	0.589	13.572	2.3E-04
Age (yrs)	1.722	0.189	1.121	0.290	0.441	0.507	0.341	0.559
Malaria exposure[1]	0.003	0.956	4.086	0.043	0.255	0.614	3.945	0.047
Gender	5.006	0.025	0.661	0.416	2.605	0.107	0.028	0.867

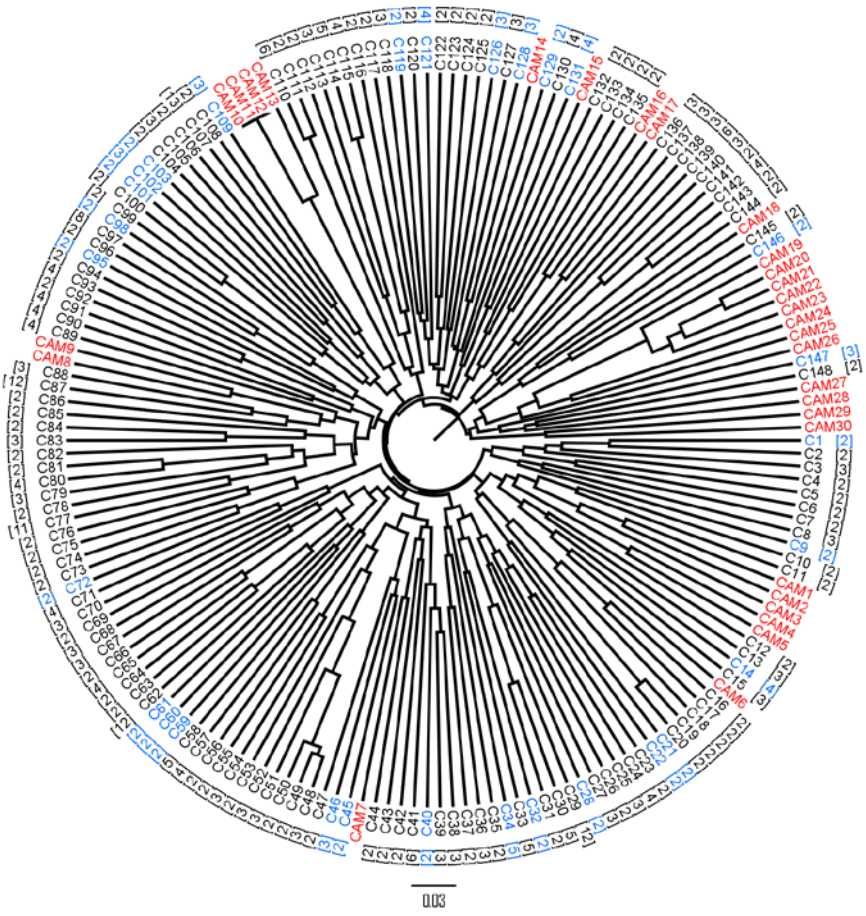
[1]Malaria exposure was defined by a documented malaria episode prior to the current episode.



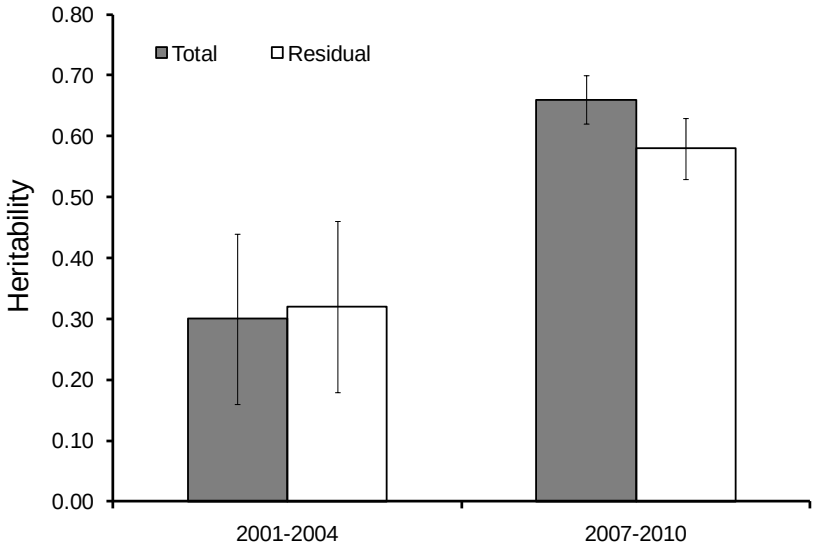
Appendix 5. Genotyping data for one SNP. A typical SNP graph for the A/T SNP on chromosome 13, position 2158308, showing clustering of samples based on their genotypes. Genotype calls are made based on the normalized ratio of fluorescence intensity signals for the "A" and the "B" allele in the sample. The X-axis shows Norm Theta values, which correspond to the composition of the "B" allele in each sample. Multiple-clone infections are easily identified and were excluded from CR heritability analysis.



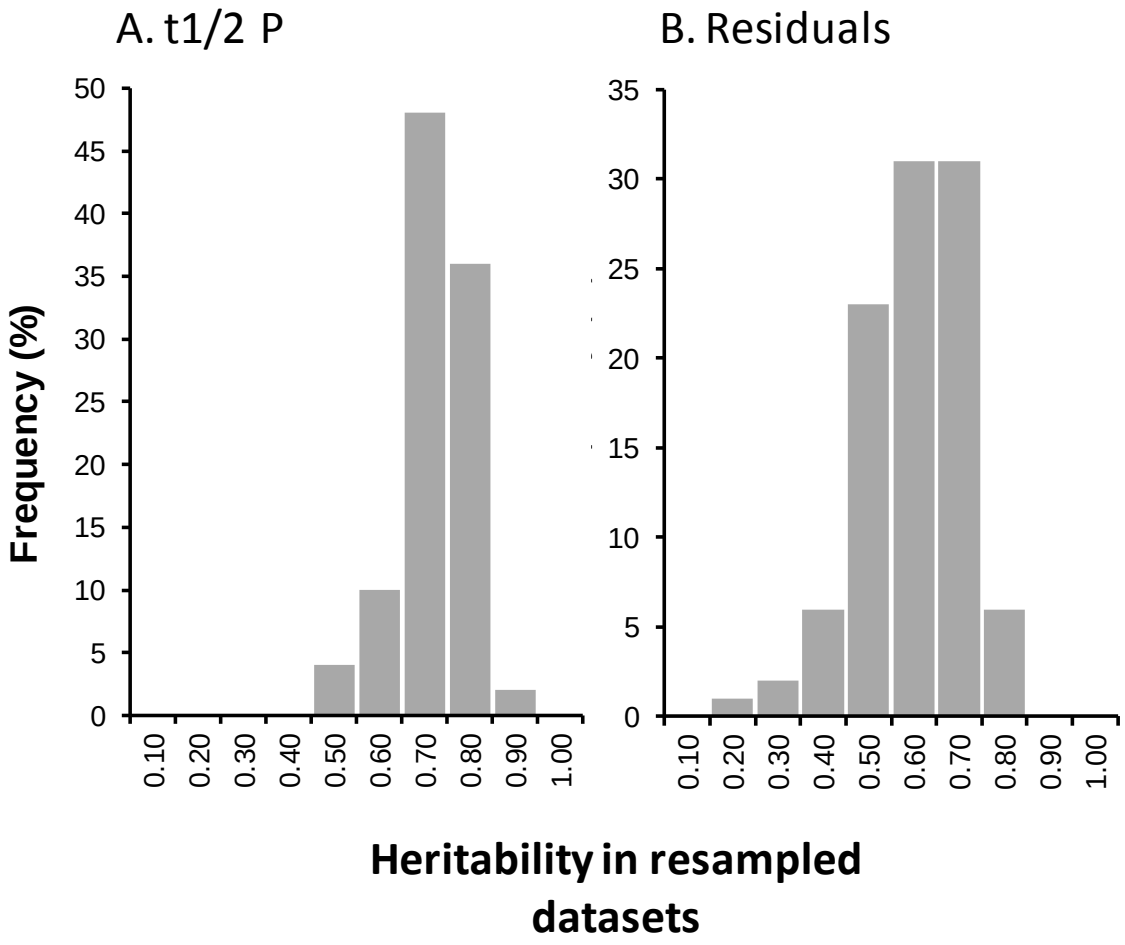
Appendix 6. Sampling breakdown for epidemiology and genetic analyses. Exclusion criteria are detailed in the text. The flow chart details how parasites with identical 93-locus genotypes infecting multiple patients were identified in the data set.



Appendix 7. Genetic relatedness among parasites. The tree shows the relatedness among 148 93-locus parasite genotypes infecting 441 patients. Blue genotype labels indicate infections collected between 2001 and 2004, black labels those collected from 2007-2010, while red labels show 30 infections from Cambodia. The numbers of patients infected with each genotype are shown in square brackets.



Appendix 8. Change in heritability of clearance rates on the Thai-Myanmar border. The proportion of variation in t½ P that is due to parasite genetic factors (heritability) is shown for 2001-4 and 2007-10 time windows. Grey bars show heritability of $t_{½}$ P, while white bars show heritability analysis of residuals after removing effects of significant covariates. The error bars are 1 SD. The increase in heritability observed between 2001-4 and 2007-10 periods were tested by permutation (Appendix 9) and were significant for both $t_{½}$ P ($p<0.01$) and residuals ($p=0.04$).



Appendix 9. Permutation-based comparison of heritability in 2001-4 and 2007-10. In 2001-4, 29 groups of patients are infected with indistinguishable parasite genotypes, while in 2007-10, there were 119 groups. We randomly resampled 250 patients from 2007-10 generating samples containing on average 29 parasite genotypes infecting >1 patient. This resampling excersise provides a direct comparison with the 2001-4 period. Heritability estimates from 100 resampled 2007-10 datasets (range=0.48-0.85 exceeded that observed in 2001-4, demonstrating that the observed increase in H^2 is significant ($p<0.01$). For residuals (following removal of effects of covariates) all but 4 resampled datasets exceeded H^2 values for 2001-4 ($p=0.04$). These analyses are shown below. The frequency distribution shows H^2 values from 100 resampled 2007-10 datasets for A. t1/2P measures and B. residuals.