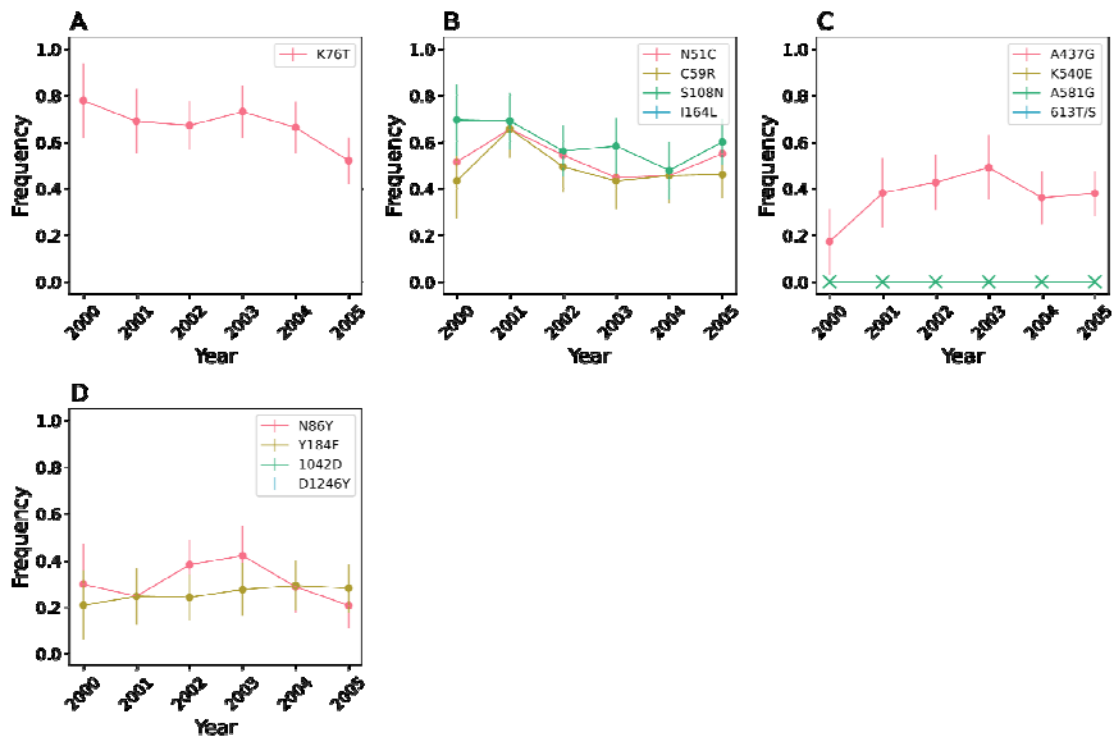


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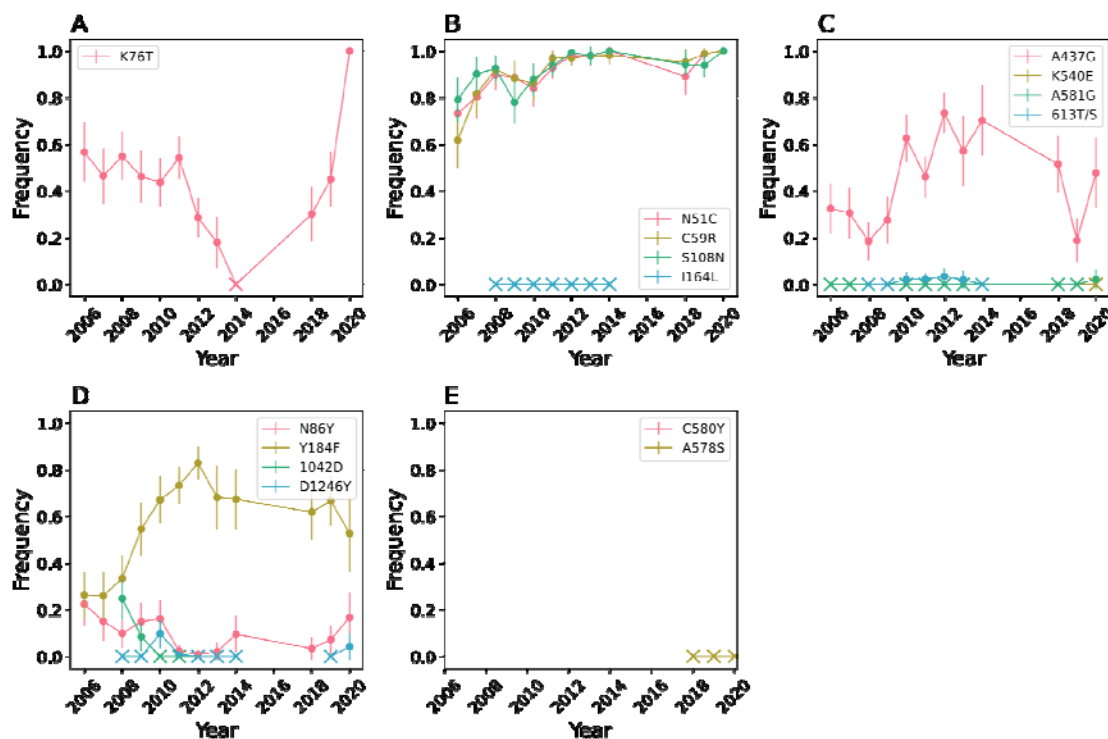
529 **Fig S1. Sample sizes for SNP-based molecular surveillance.** Sample size per year per
 530 region for the SNP-based molecular surveillance.

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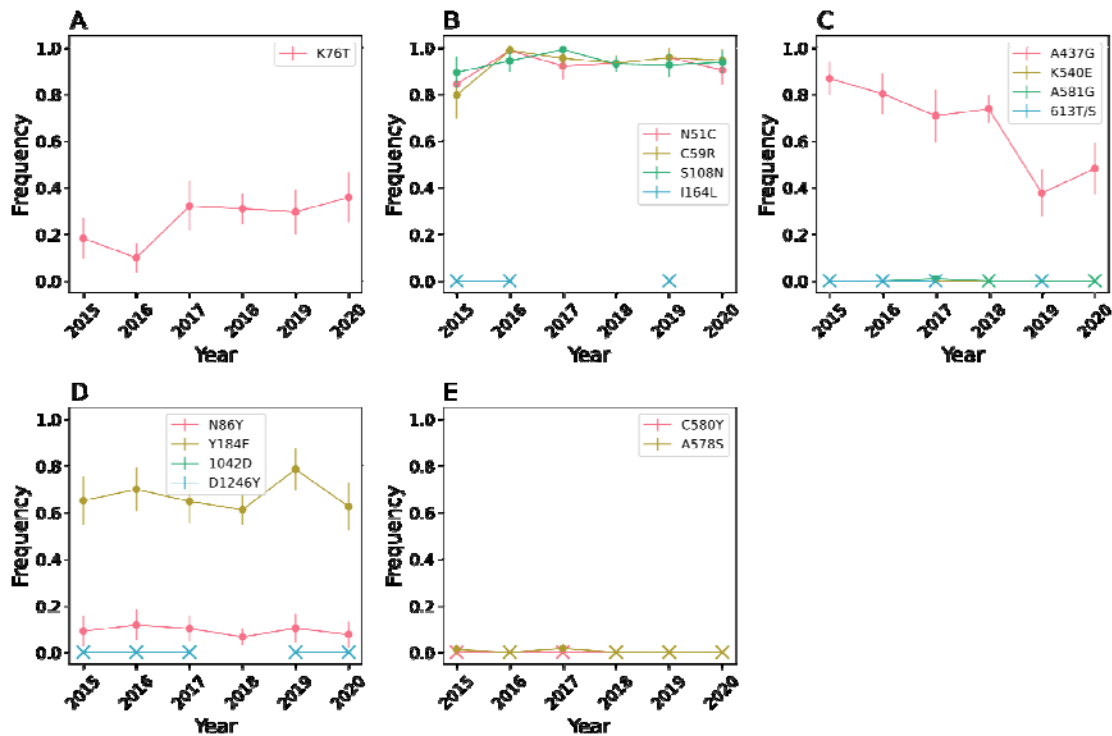
533 **Fig S2. SNP-based molecular surveillance in Pikine** for A) *Pfcrtr*, B) *Pfdhfr*, C) *Pfdhps* and
534 D) *Pfmdr1*. The *Pfkelch13* SNPs were not examined in Pikine. Error bars indicate two
535 binomial standard deviations from the mean. X's denote years where samples were collected
536 but the mutation was not observed. Gaps in the data were because samples were not
537 collected for that year.



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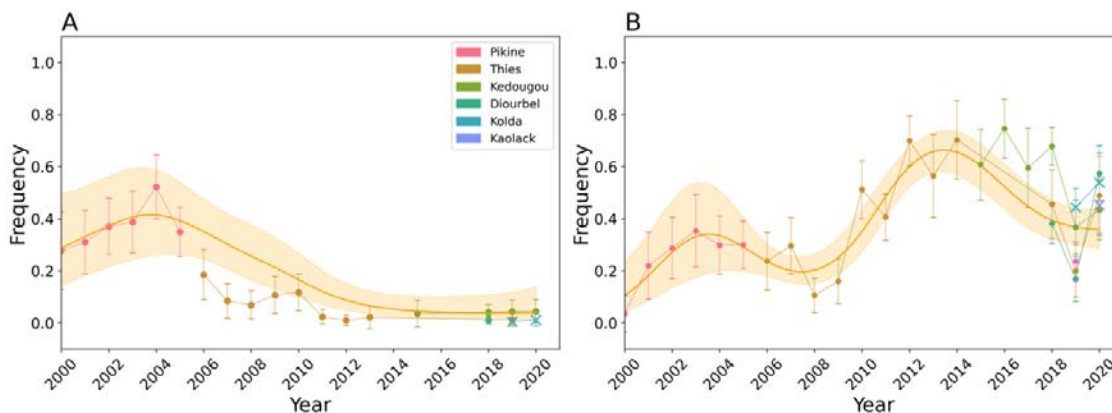
539 **Fig S3. SNP-based molecular surveillance in Thies** for A) *Pfcrtr*, B) *Pfdhfr*, C) *Pfdhps* and
540 D) *Pfmdr1*, and E) *Pfkelch13*. Error bars indicate two binomial standard deviations from the
541 mean. X's denote years where samples were collected but the mutation was not observed.
542 Gaps in the data were because samples were not collected for that year.

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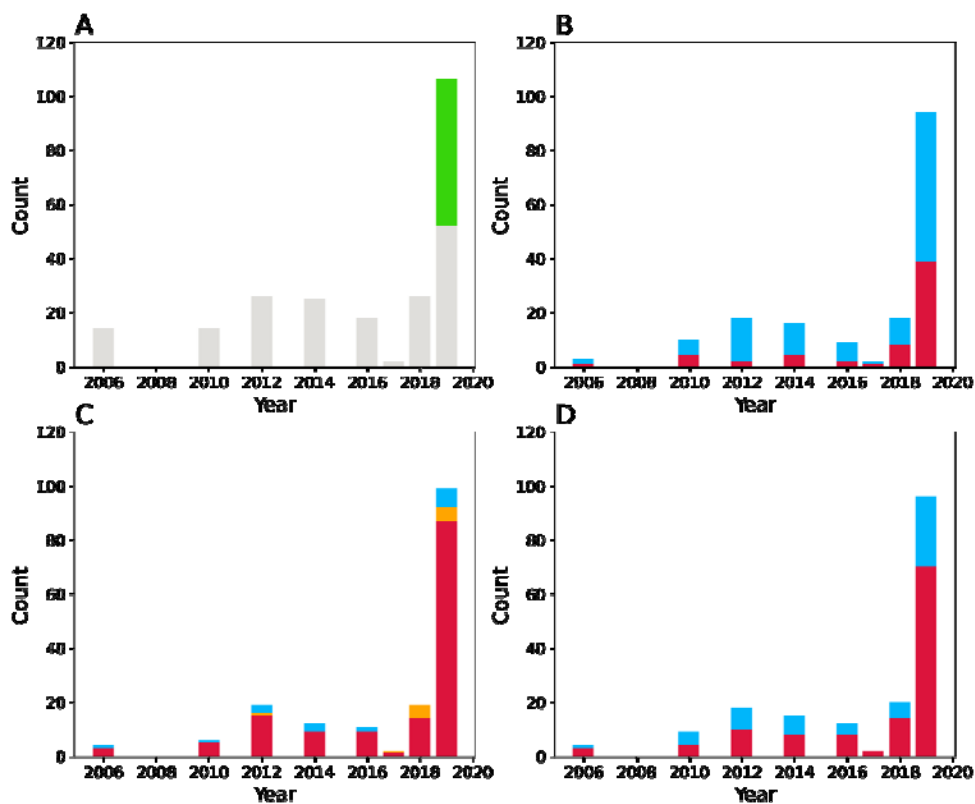
545 **Fig S4. SNP-based molecular surveillance in Kedougou for A) *Pfcrtr*, B) *Pfdhfr*, C)**
 546 *Pfdhps*, D) *Pfmdr1*, and E) *Pfkelch13*. Error bars indicate two binomial standard deviations
 547 from the mean. X's denote years where samples were collected but the mutation was not
 548 observed. Gaps in the data were because samples were either not collected or not
 549 genotyped for that year.



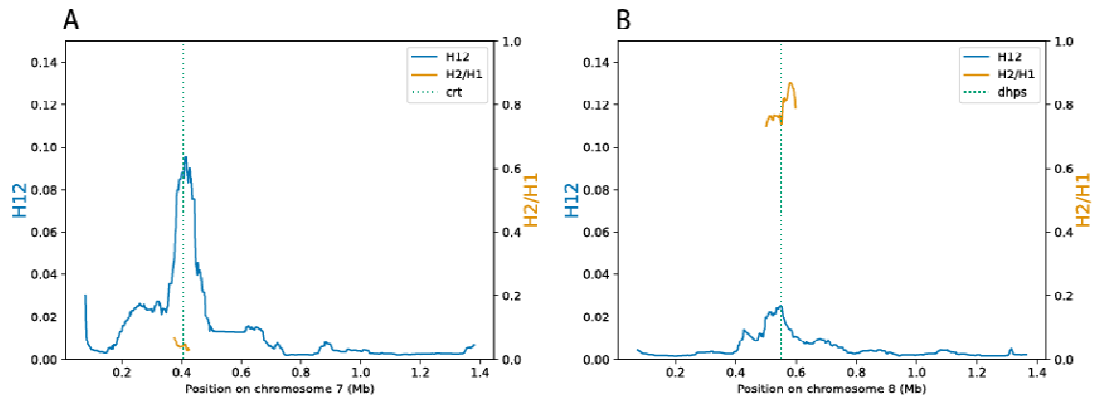
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551 **Fig S5. A)** Frequency of *Pf dhfr* triple sensitive (N51, C59, S108) parasites. **B)** Frequency of
 552 “quadruple” (*Pf dhfr* triple mutant + *Pfdhps* A437G) parasites. The scatterplots show the
 553 observed frequencies and their 95% binomial confidence interval. Model predictions from a
 554 calibrated generalized additive model and the 95% confidence intervals are shown in orange.
 555 The model was calibrated with data from Pikine, Thiès, Diourbel, and Kedougou (denoted

556 with circles). The data from Kolda and Kaolack (denoted with X) were not used for model
557 calibration.

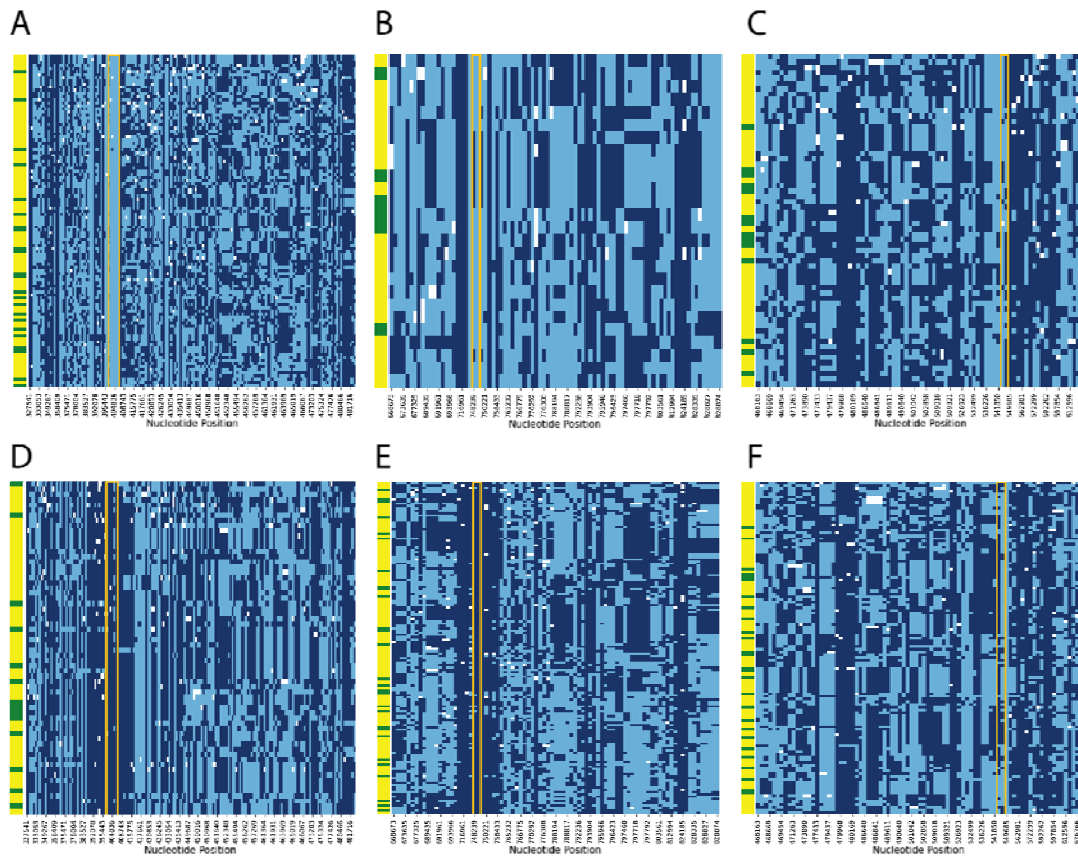


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559 **Fig S6 Sampling distribution for our whole genome sequence collection (A).** Grey
560 indicates the sample came from Thiès. Green indicates the sample came from Kedougou.
561 Sampling distributions for **B)** the *Pfcr* genomic region, **C)** the *Pfdhfr* genomic region, and **D)**
562 the *Pfdhps* genomic regions. For **B** and **D**, blue denotes samples with the sensitive allele and
563 red indicates those with the resistance allele. For **C**, red denotes samples that are *Pfdhfr*
564 triple mutant, blue indicates those that are *Pfdhfr* triple sensitive, and orange indicates those
565 with a mix of resistant and sensitive alleles at the three examined *Pfdhfr* loci.
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Fig S7 Evidence of Hard and Soft Sweeps H12 (*blue*, left y-axis) and H2/H1 (*orange*, right y-axis) statistics for **A)** chromosome 7 and **B)** chromosome 8. The dotted green lines show the location of *Pfcrt* or *Pfdhps*.



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Fig S8. SNPs used to define genomic haplotypes. Genomic haplotypes surrounding the wild-type mutations: **A)** *Pfcrt* K76, **B)** *Pfdhfr* C59, **C)** *Pfdhps* A437 and the drug resistance mutations: **D)** *Pfcrt* K76T, **E)** *Pfdhfr* C59R, **F)** *Pfdhps* A437G. Each row represents a sample. The left most column indicates whether the sample was collected before 2014 (*green*) or

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578 after 2014 (*yellow*). Alleles corresponding to the 3D7 reference are indicated by *light blue*
579 and alleles corresponding to the alternative allele are indicated by *dark blue*. White
580 corresponds to missing data. The orange boxes highlight the boundaries of the *Pfcr* (**A/D**),
581 *Pfdhfr* (**B/E**), and *Pfdhps* (**C/F**) genes,

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