Additional file

The landscape of drug resistance in *Plasmodium falciparum* malaria in the Democratic Republic of Congo: a mapping systematic review

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Contents

Table S1: PRISMA checklist [1] for the review of malaria drug resistance in the Democratic Republic of Congo.

Section/topic	#	Checklist item	Reported on page #
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5; Additional file p.4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4-5; Additional file p.4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6; Additional file p.4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6-7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Additional file p.5
Results of individual studies	20	For all outcomes considered (benefits or harms), present for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Additional file p.5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies.	Additional file p.5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

Table S2. Strategy used to search for articles published and included in the study.

#1	(Malaria OR paludisme OR *Plasmodium*)
#2	("molecular marker" OR "marqueur moléculaire" OR *mdr1* OR *Pfmdr1* OR *Pfmdr2* OR *crt* OR *Pfcrt* OR *kelch13* OR *Pfkelch13* OR K13 OR *dhfr* OR *Pfdhfr* OR *dhps* OR *Pfdhps* OR *Pfpm3* OR *pm3* OR *Pfpm2* OR *pm2* OR *Pfcytb* OR *cytb* OR *Pfnhe1* OR *nhe1*) AND (resistance OR résistance OR resistant OR résistant)
#3	("Democratic Republic of Congo" OR "République Démocratique du Congo" OR Zaïre OR Congo)
Search	#1 AND #2 AND #3

Table S3. PICOS criteria for the selection of primary articles published before July 2023.

Parameters	**Inclusion criteria**	**Exclusion criteria**
Population	• Individuals residing in the DRC and having been infected with malaria parasites.	• Traveling malaria cases detected outside the DRC.
Intervention	• Detection of *Plasmodium* parasites by PCR technique on blood samples with genotyping of any genes putatively involved in antimalarial drug resistance (i.e., *kelch13*, *mdr1*, *mdr2*, *crt*, *dhfr*, *dhps*, *pm3*, *pm2*, *cytb* and *nhe1*).	• No report on genes involved in antimalarial drug resistance
Comparator	• Criteria not applicable for this review.	• Criteria not applicable for this review
Outcomes	• Genotype of at least one locus on one of the following genes: *kelch13*, *mdr1*, *mdr2*, *crt*, *dhfr*, *dhps*, *pm3*, *pm2*, *cytb* and *nhe1*	• No reported data on genotypes and number of genotyped isolates
Study Design	• Peer-reviewed observational or clinical trial articles reporting on newly analyzed *Plasmodium* isolates	• Letters, commentaries, conference summaries, conference presentations; • Systematic reviews and meta-analyzes; • Studies based exclusively on animal models; • Data relating to *Plasmodium* isolates genetically modified during laboratory experiments.

Table S4. Basic characteristics of articles included in this review article.

N°	Article	Data collection period	No. of sites	No. of samples	Analyzed molecular marker of drug resistance	Quality level
1	Alker AP et al. 2008 [2]	2002	1	249	*Pf*DHFR, *Pf*DHPS	Moderate
2	Antonia AL et al. 2014 [3]	2007	Unkown	180	*Pf*CRT	Moderate
3	Baraka V et al. 2017 [4]	2012-2014	1	37	*Pf*DHPS	Moderate
4	Baraka V et al. 2018 [5]	2012-2014	1	2265	*Pf*MDR1	Moderate
5	Cohuet S et al. 2006 [6]	2003-2004	3	458	*Pf*DHFR, *Pf*DHPS	Moderate
6	Deutsch-Feldman M et al. 2019 [7]	2013-2014, 2007	Unkown	852	*Pf*DHFR, *Pf*CRT	Moderate
7	Kamau E et al. 2015 [8]	2013-2014	1	82	*Pf*K13	Moderate
8	Kayiba NK et al. 2021 [9]	2018-2019	1	844	*Pf*DHPS, *Pf*DHFR	Moderate
9	Leroy D et al. 2019 [10]	2014-2015	1	5	*Pf*K13	Moderate
10	Menard D et al. 2016 [11]	2009-2014	Unkown	1288	*Pf*K13	Moderate
11	Mens PF et al. 2008 [12]	2003-2004	1	78	*Pf*DHPS	Moderate
12	Miotto O et al. 2015 [13]	2009-2010	1	115	*Pf*K13	Moderate
13	Mobula L et al. 2009 [14]	2008	1	142	*Pf*CRT, *Pf*MDR1, *Pf*DHFR, *Pf*DHPS	Moderate
14	Moriarty LF et al. 2021 [15]	2017-2018	5	523	*Pf*CRT, *Pf*K13, *Pf*MDR1	Moderate
15	Mvumbi DM et al. 2013[16]	2010	1	145	*Pf*CRT	Moderate
16	Mvumbi DM et al. 2017 [17]	2014	6	280	*Pf*K13	Moderate
17	Nkoli Mandoko P et al. 2018 [18]	2014-2015	2	2030	*Pf*DHFR, *Pf*DHPS	Moderate
18	Nundu SS et al. 2022 [19]	2019	1	229	*Pf*K13, *Pf*MDR1, *Pf*DHFR, *Pf*DHPS, *Pf*CRT	Moderate
19	Ruh E et al. 2018 [20]	2014	1	48	*Pf*DHFR, *Pf*DHPS	Moderate
20	Severini C et al. 2006 [21]	2000	1	27	*Pf*CRT	Moderate
21	Swarthout TD et al. 2006 [22]	2003	1	217	*Pf*DHFR, *Pf*DHPS	Moderate
22	Taylor SM et al. 2014 [23]	2007	11	179	*Pf*DHPS	Moderate
23	Taylor SM et al. 2015 [24]	2007	3	151	*Pf*K13	Moderate
24	van Lenthe M et al. 2019 [25]	2017	4	1086	*Pf*DHFR, *Pf*DHPS	Moderate
25	Wilson PE et al. 2005 [26]	2002	1	56	*Pf*CRT	Moderate
26	Yobi DM et al. 2020a [27]	2017	10	1070	*Pf*K13	Moderate
27	Yobi DM et al. 2020b [28]	2017	10	1070	*Pf*CRT	Moderate
28	Yobi DM et al. 2021 [29]	2018-2019	6	474	*Pf*CRT, *Pf*K13, *Pf*MDR1	Moderate
29	Yobi DM et al. 2022 [30]	2019-2020	10	1087	*Pf*CRT, *Pf*K13	Moderate

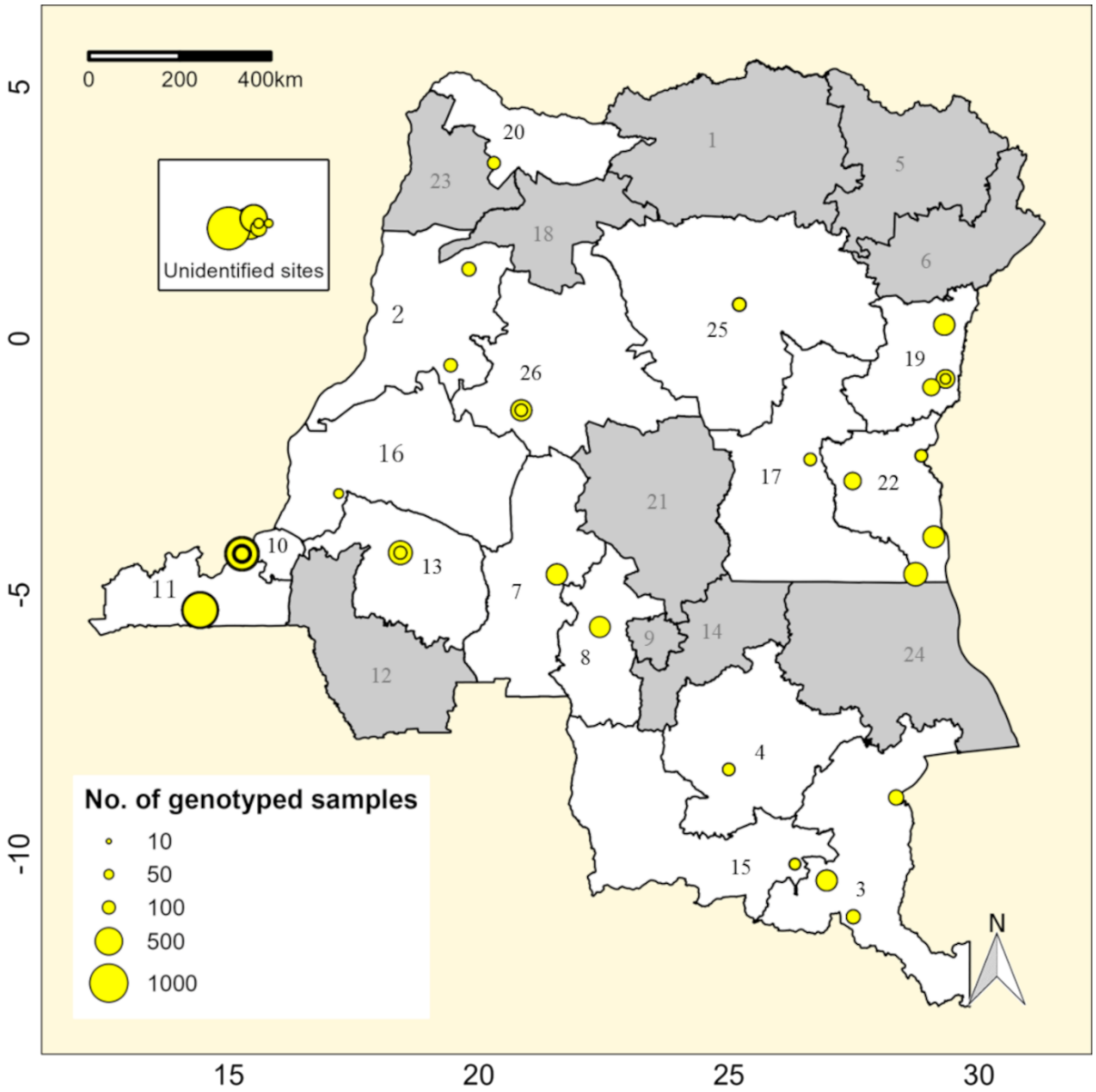

Figure S1. Geographic locations of collection sites in primary studies.

The location of each primary survey has been uploaded onto this map. Shaded areas represent the country's provinces that were not surveyed during this review. Yellow circles reflect individual surveys conducted at different locations with a diameter proportional to the size of the samples that were successfully investigated for molecular markers of antimalarial drug resistance. The numbers written on the map represent the 26 provinces of the country as follows: Bas-Uele : 1; Equateur : 2; Haut-Katanga : 3; Haut-Lomami : 4; Haut-Uele : 5; Ituri : 6; Kasai : 7; Kasai-Central : 8; Kasai-Oriental : 9; Kinshasa :10; Kongo-Central : 11; Kwango : 12; Kwilu : 13; Lomami : 14; Lualaba : 15; Mai-Ndombe : 16; Maniema : 17; Mongala : 18; Nord-Kivu : 19; Nord-Ubangi : 20; Sankuru : 21; Sud-Kivu : 22; Sud-Ubangi : 23; Tanganyika : 24; Tshopo : 25; and Tshuapa : 26.

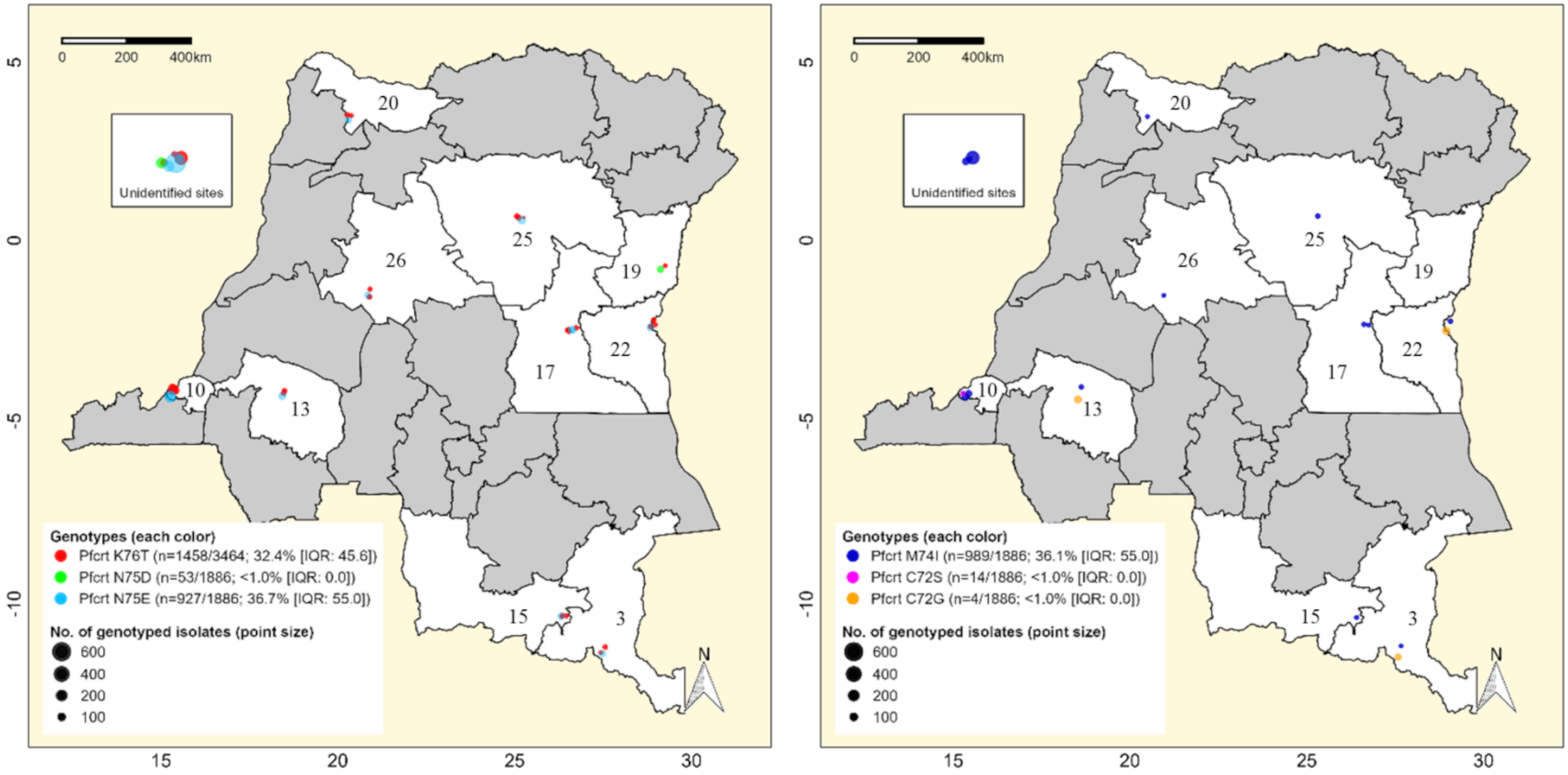

Figure S2. Distribution of parasites carrying different *Pf*CRT mutations.

Circles displayed on these maps reflect surveys that reported at least one parasite carrying a mutation on *Pf*CRT 72-76 codon-positions. The diameter of each circle is proportional to the number of isolates for which the corresponding *Pf*CRT 72-76 codon-position has been successfully genotyped. Individual mutations are reported with absolute frequencies and relative proportions across different surveyed sites. Shaded areas reflect provinces that have not been monitored for parasites harboring *Pf*CRT 72-76 mutations. The numbers written on the map represent the 26 provinces of the country as follows: Haut-Katanga : 3; Kinshasa :10; Kwilu : 13; Lualaba : 15; Maniema : 17; Nord-Kivu : 19; Nord-Ubangi : 20; Sud-Kivu : 22; Tshopo : 25; and Tshuapa : 26.

Table S5. Evolution of the frequency of parasite carrying a *Pf*CRT K76T mutation in the DRC.*

Sampling year	n	m	Median % of *Pf*CRT K76T isolates (IQR)
2000	27	27	100 (0.0)
2002	56	52	92.9 (0.0)
2007	841	461	55.0 (0.4)
2008	105	88	83.8 (0.0)
2010	198	145	73.2 (0.0)
2017	849	218	11.3 (40.5)
2018	335	139	33.6 (22.1)
2019	1053	199	13.3 (23.2)

(*) n: No. of genotyped isolates; m: No. of detected mutants

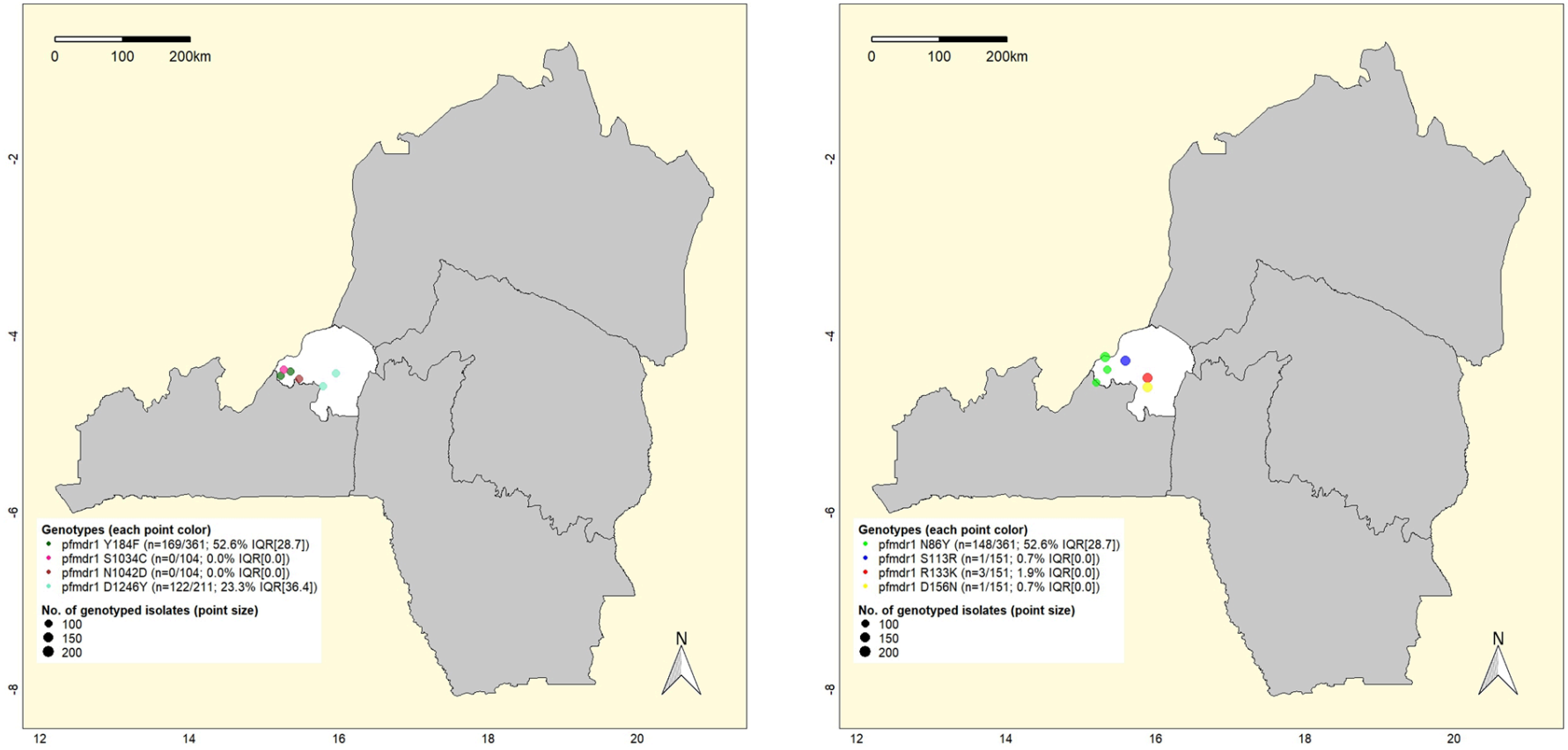

Figure S3. Distribution of parasites carrying *Pfmdr*1 SNPs in the DRC.

Each survey having explored parasites carrying different *Pfmdr1* mutations were uploaded on these two maps. These parasites were explored only in Kinshasa, the country&s capital city (shown here as an unshaded area). Circles represent surveys conducted at different locations with a diameter proportional to the sample size of isolates that have been successfully analyzed for the corresponding alteration. The colors differentiate the different *Pfmdr1* mutations sought and for which the median frequencies and the respective interquartile ranges are presented.

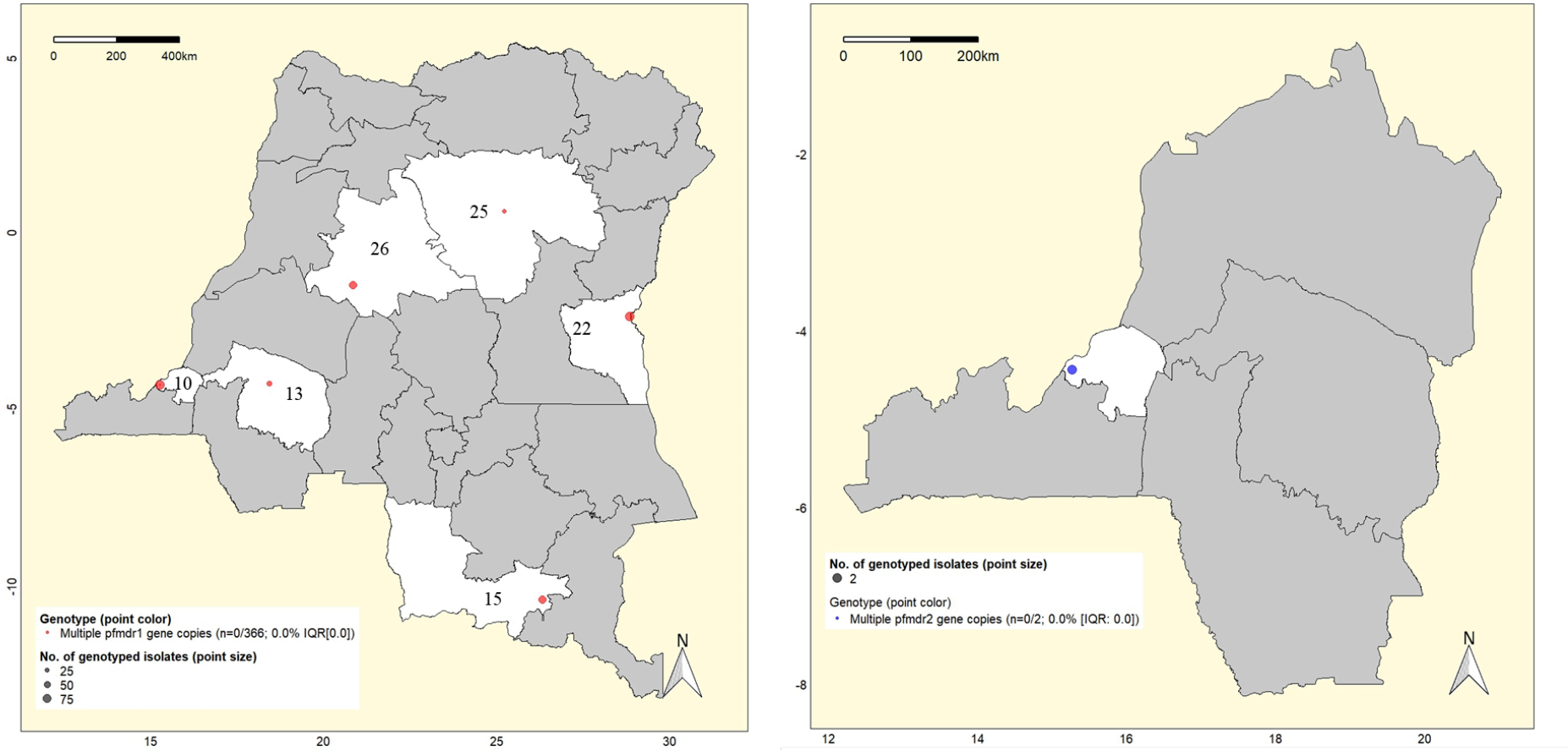

Figure S4. Distribution of parasites genotyped for *Pfmdr*1 and *Pfmdr2* gene copy number alterations in the DRC.

Each survey having genotyped parasites for potential alterations in *Pfmdr1* and *Pfmdr1* gene copy numbers were uploaded on these two maps. Unshaded areas are provinces that have been explored for these parasites (Kinshasa :10; Kwilu : 13; Lualaba : 15; Sud-Kivu : 22; Tshopo : 25; and Tshuapa : 26). Circles reflect surveys conducted at different locations with a diameter proportional to the sample size of isolates that have been successfully analyzed for the gene alterations. The colors differentiate the different genes explored for which the number of isolates, the median frequencies and the respective interquartile ranges are presented.

Table S6. Overall proportions of parasites carrying non-synonymous mutations of the *Pf*K13 in the DRC*

Locus	NS mutation	n	m	%
92	K92N	79	2	2,5
149	T149S	79	4	5,1
189	K189T	79	20	25,3
255	R255K	79	4	5,1
472	M472I	5383	1	0,0
472	M472L	5383	1	0,0
473	C473Y	5383	1	0,0
476	M476K	5383	1	0,0
477	S477Y	5383	1	0,0
495	F495L	5383	2	0,0
498	N498I	5383	1	0,0
506	F506L	5383	1	0,0
507	E507V	5383	1	0,0
509	E509D	5383	2	0,0
516	D516A	5383	1	0,0
516	D516E	5383	1	0,0
520	V520A	5383	4	0,1
522	S522C	5383	2	0,0
523	N523T	5383	1	0,0
532	C532S	5383	1	0,0
534	V534A	5383	4	0,1
538	G538S	5383	1	0,0
554	N554K	5383	2	0,0
557	A557S	5383	3	0,1
561	R561H	5383	2	0,0
567	E567K	5383	1	0,0
568	V568M	5383	1	0,0
569	A569T	5383	1	0,0
576	S576T	5383	1	0,0
578	A578S	5383	10	0,2
584	D584E	5383	2	0,0
588	Y588C	5383	1	0,0
596	E596K	5383	1	0,0
613	Q613E	5383	3	0,1

(*) n: No. of genotyped isolates; m: No. of detected mutants; %: overall proportion of mutants; loci beyond 442 are located in the propeller domain.

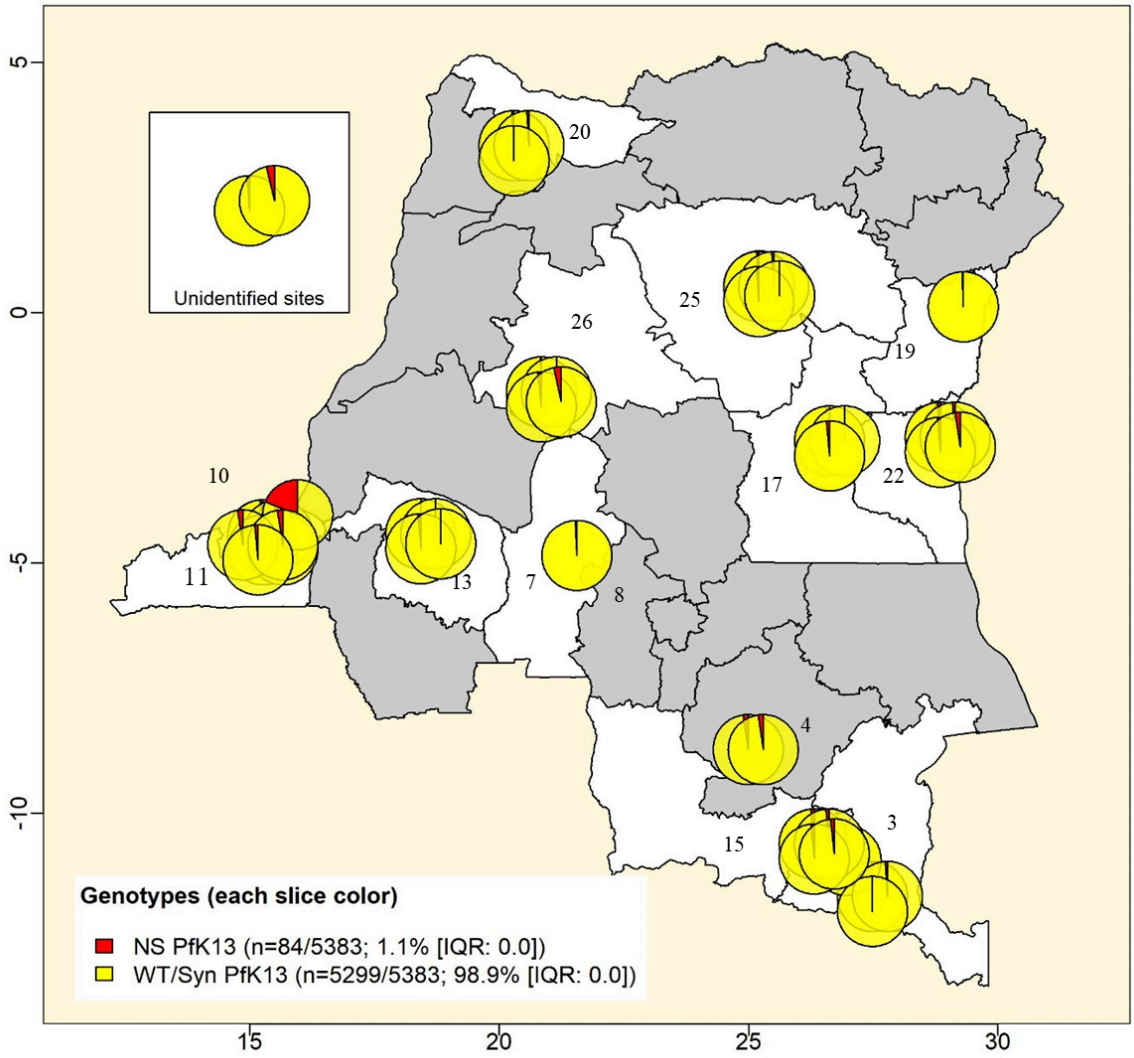

Figure S5 Distribution of *Plasmodium* parasites carrying non-synonymous *Pf*K13 mutations in the DRC.

The pie charts displayed on these maps represent the proportions of isolates carrying at least one non-synonymous *Pf*K13 mutation (NS, portion colored in red) and those of isolates carrying a wild-type *Pf*K13 sequence or with only synonyms mutations (WT/Syn, portion colored in yellow). The numbers written on the map represent differents provinces that have been explored so far for these parasites: Haut-Katanga : 3; Haut-Lomami : 4; Kasai : 7; Kasai-Central : 8; Kinshasa :10; Kongo-Central : 11; Maniema : 17; Nord-Kivu : 19; Nord-Ubangi : 20; Sud-Kivu : 22; Tshopo : 25; and Tshuapa : 26.

Table S7. Overall proportions of parasites encoding different *Pfdhfr-Pfdhps* haplotypes in the DRC*

Haplotype	n	m	%
Wild-type haplotype			
NCS-AK (i.e., *Pfdhfr* N51, C59, S108; *Pfdhps* A437, K540)	2092	9	0,7
Mutant haplotypes			
IRN-AE (i.e., *Pfdhfr* N51I, C59R, S108N; *Pfdhps* A437, K540E)	2092	1	0,0
NCS-GK (i.e., *Pfdhfr* N51, C59, S108; *Pfdhps* A437G, K540)	2092	1	0,0
NCN-GK (i.e., *Pfdhfr* N51, C59, S108N; *Pfdhps* A437G, K540)	2092	2	0,1
NRN-AK (i.e., *Pfdhfr* N51, C59R, S108N; *Pfdhps* A437, K540)	2092	2	0,1
NCS-GE (i.e., *Pfdhfr* N51, C59, S108; *Pfdhps* A437G, K540E)	2092	3	0,1
ICN-AK (i.e., *Pfdhfr* N51I, C59, S108N; *Pfdhps* A437, K540)	2092	6	0,3
ICN-GE (i.e., *Pfdhfr* N51I, C59, S108N; *Pfdhps* A437G, K540E)	2092	16	0,8
NRN-GK (i.e., *Pfdhfr* N51, C59R, S108N; *Pfdhps* A437G, K540)	2092	17	0,8
IRN-AK (i.e., *Pfdhfr* N51I, C59R, S108N; *Pfdhps* A437, K540)	2092	19	0,9
ICN-GK (i.e., *Pfdhfr* N51I, C59, S108N; *Pfdhps* A437G, K540)	2092	139	6,6
IRN-GE (i.e., *Pfdhfr* N51I, C59R, S108N; *Pfdhps* A437G, K540E)	2092	320	13,1
IRN-GK (i.e., *Pfdhfr* N51I, C59R, S108N; *Pfdhps* A437G, K540)	2092	1018	59,3
Unspecified	2092	539	21,8

(*) n: No. of genotyped isolates; m: No. of detected mutants; %: median proportion of mutants

References

1. Takkouche B, Norman G: **PRISMA statement**. *Epidemiology* 2011, **22**(1):128.
2. Alker AP, Kazadi WM, Kutelemeni AK, Bloland PB, Tshefu AK, Meshnick SR: **dhfr and dhps genotype and sulfadoxine‐pyrimethamine treatment failure in children with falciparum malaria in the Democratic Republic of Congo**. *Tropical Medicine & International Health* 2008, **13**(11):1384-1391.
3. Antonia AL, Taylor SM, Janko M, Emch M, Tshefu AK, Meshnick SR: **A cross-sectional survey of Plasmodium falciparum pfcrt mutant haplotypes in the Democratic Republic of Congo**. *The American journal of tropical medicine and hygiene* 2014, **90**(6):1094-1097.
4. Baraka V, Delgado-Ratto C, Nag S, Ishengoma DS, Madebe RA, Mavoko HM, Nabasumba C, Lutumba P, Alifrangis M, Van Geertruyden J-P: **Different origin and dispersal of sulfadoxine-resistant Plasmodium falciparum haplotypes between Eastern Africa and Democratic Republic of Congo**. *International journal of antimicrobial agents* 2017, **49**(4):456-464.
5. Baraka V, Mavoko HM, Nabasumba C, Francis F, Lutumba P, Alifrangis M, Van Geertruyden J-P: **Impact of treatment and re-treatment with artemether-lumefantrine and artesunate-amodiaquine on selection of Plasmodium falciparum multidrug resistance gene-1 polymorphisms in the Democratic Republic of Congo and Uganda**. *PLoS One* 2018, **13**(2):e0191922.
6. Cohuet S, Bonnet M, Van Herp M, Van Overmeir C, D'Alessandro U, Guthmann J-P: **molecular markers associated with Plasmodium falciparum resistance to sulfadoxine-pyrimethamine in the Democratic Republic of Congo**. 2006.
7. Deutsch-Feldman M, Aydemir O, Carrel M, Brazeau NF, Bhatt S, Bailey JA, Kashamuka M, Tshefu AK, Taylor SM, Juliano JJ: **The changing landscape of Plasmodium falciparum drug resistance in the Democratic Republic of Congo**. *BMC infectious diseases* 2019, **19**(1):1-10.
8. Kamau E, Campino S, Amenga-Etego L, Drury E, Ishengoma D, Johnson K, Mumba D, Kekre M, Yavo W, Mead D: **K13-propeller polymorphisms in Plasmodium falciparum parasites from sub-Saharan Africa**. *The Journal of infectious diseases* 2015, **211**(8):1352-1355.
9. Kayiba NK, Yobi DM, Kouoneyou VRT, Mvumbi DM, Kabututu PZ, Devleesschauwer B, Sompwe EM, DeMol P, Hayette M-P, Mvumbi GL: **Evaluation of the usefulness of intermittent preventive treatment of malaria in pregnancy with sulfadoxine-pyrimethamine in a context with increased resistance of Plasmodium falciparum in Kingasani Hospital, Kinshasa in the Democratic Republic of Congo**. *Infection, Genetics and Evolution* 2021:105009.
10. Leroy D, Macintyre F, Adoke Y, Ouoba S, Barry A, Mombo-Ngoma G, Ngomo JMN, Varo R, Dossou Y, Tshefu AK: **African isolates show a high proportion of multiple copies of the Plasmodium falciparum plasmepsin-2 gene, a piperaquine resistance marker**. *Malaria journal* 2019, **18**(1):1-11.
11. Ménard D, Khim N, Beghain J, Adegnika AA, Shafiul-Alam M, Amodu O, Rahim-Awab G, Barnadas C, Berry A, Boum Y: **A worldwide map of Plasmodium falciparum K13-propeller polymorphisms**. *New England Journal of Medicine* 2016, **374**(25):2453-2464.
12. Mens PF, van Overmeir C, Bonnet M, Dujardin JC, d'Alessandro U: **Real-time PCR/MCA assay using fluorescence resonance energy transfer for the genotyping of resistance related DHPS-540 mutations in Plasmodium falciparum**. *Malar J* 2008, **7**:48.
13. Miotto O, Amato R, Ashley EA, MacInnis B, Almagro-Garcia J, Amaratunga C, Lim P, Mead D, Oyola SO, Dhorda M: **Genetic architecture of artemisinin-resistant Plasmodium falciparum**. *Nature genetics* 2015, **47**(3):226-234.
14. Mobula L, Lilley B, Tshefu AK, Rosenthal PJ: **Resistance-mediating polymorphisms in Plasmodium falciparum infections in Kinshasa, Democratic Republic of the Congo**. *The American journal of tropical medicine and hygiene* 2009, **80**(4):555-558.
15. Moriarty LF, Nkoli PM, Likwela JL, Mulopo PM, Sompwe EM, Rika JM, Mavoko HM, Svigel SS, Jones S, Ntamabyaliro NY *et al*: **Therapeutic Efficacy of Artemisinin-Based Combination Therapies in Democratic Republic of the Congo and Investigation of Molecular Markers of Antimalarial Resistance**. *The American journal of tropical medicine and hygiene* 2021, **105**(4):1067-1075.
16. Mvumbi DM, Boreux R, Sacheli R, Lelo M, Lengu B, Nani-Tuma S, Melin P, Ntumba K, Lunganza K, DeMol P *et al*: **Assessment of pfcrt 72-76 haplotypes eight years after chloroquine withdrawal in Kinshasa,**

Democratic Republic of Congo. *Malar J* 2013, **12**:459.

17. Mvumbi DM, Bobanga TL, Kayembe JN, Mvumbi GL, Situakibanza HN, Benoit-Vical F, Melin P, De Mol P, Hayette MP: **Molecular surveillance of Plasmodium falciparum resistance to artemisinin-based combination therapies in the Democratic Republic of Congo**. *PLoS One* 2017, **12**(6):e0179142.
18. Nkoli Mandoko P, Rouvier F, Matendo Kakina L, Moke Mbongi D, Latour C, Losimba Likwela J, Ngoyi Mumba D, Bi Shamamba SK, Tamfum Muyembe J-J, Muepu Tshilolo L: **Prevalence of Plasmodium falciparum parasites resistant to sulfadoxine/pyrimethamine in the Democratic Republic of the Congo: emergence of highly resistant pfdhfr/pfdhps alleles**. *Journal of Antimicrobial Chemotherapy* 2018, **73**(10):2704-2715.
19. Nundu SS, Culleton R, Simpson SV, Arima H, Chitama BA, Muyembe JJ, Ahuka S, Kaneko O, Mita T, Yamamoto T: **Identification of polymorphisms in genes associated with drug resistance in Plasmodium falciparum isolates from school-age children in Kinshasa, Democratic Republic of Congo**. *Parasitology international* 2022, **88**:102541.
20. Ruh E, Bateko JP, Imir T, Taylan-Ozkan A: **Molecular identification of sulfadoxine-pyrimethamine resistance in malaria infected women who received intermittent preventive treatment in the Democratic Republic of Congo**. *Malar J* 2018, **17**(1):17.
21. Severini C, Menegon M, Sannella AR, Paglia MG, Narciso P, Matteelli A, Gulletta M, Caramello P, Canta F, Xayavong MV: **Prevalence of pfcrt point mutations and level of chloroquine resistance in Plasmodium falciparum isolates from Africa**. *Infection, Genetics and Evolution* 2006, **6**(4):262-268.
22. Swarthout TD, van den Broek IV, Kayembe G, Montgomery J, Pota H, Roper C: **Artesunate + amodiaquine and artesunate + sulphadoxine-pyrimethamine for treatment of uncomplicated malaria in Democratic Republic of Congo: a clinical trial with determination of sulphadoxine and pyrimethamine-resistant haplotypes**. *Tropical medicine & international health : TM & IH* 2006, **11**(10):1503-1511.
23. Taylor SM, Antonia AL, Harrington WE, Goheen MM, Mwapasa V, Chaluluka E, Fried M, Kabyemela E, Madanitsa M, Khairallah C *et al*: **Independent lineages of highly sulfadoxine-resistant Plasmodium falciparum haplotypes, eastern Africa**. *Emerging infectious diseases* 2014, **20**(7):1140-1148.
24. Taylor SM, Parobek CM, DeConti DK, Kayentao K, Coulibaly SO, Greenwood BM, Tagbor H, Williams J, Bojang K, Njie F *et al*: **Absence of putative artemisinin resistance mutations among Plasmodium falciparum in Sub-Saharan Africa: a molecular epidemiologic study**. *J Infect Dis* 2015, **211**(5):680-688.
25. van Lenthe M, van der Meulen R, Lassovski M, Ouabo A, Bakula E, Badio C, Cibenda D, Okell L, Piriou E, Grignard L *et al*: **Markers of sulfadoxine-pyrimethamine resistance in Eastern Democratic Republic of Congo; implications for malaria chemoprevention**. *Malar J* 2019, **18**(1):430.
26. Wilson PE, Kazadi W, Kamwendo DD, Mwapasa V, Purfield A, Meshnick SR: **Prevalence of pfcrt mutations in Congolese and Malawian Plasmodium falciparum isolates as determined by a new Taqman assay**. *Acta tropica* 2005, **93**(1):97-106.
27. Yobi DM, Kayiba NK, Mvumbi DM, Boreux R, Bontems S, Kabututu PZ, De Mol P, Speybroeck N, Mvumbi GL, Hayette MP: **The lack of K13-propeller mutations associated with artemisinin resistance in Plasmodium falciparum in Democratic Republic of Congo (DRC)**. *PLoS One* 2020, **15**(8):e0237791.
28. Yobi DM, Kayiba NK, Mvumbi DM, Boreux R, Kabututu PZ, Situakibanza HNT, Likwela JL, De Mol P, Okitolonda EW, Speybroeck N *et al*: **Molecular surveillance of anti-malarial drug resistance in Democratic Republic of Congo: high variability of chloroquinoresistance and lack of amodiaquinoresistance**. *Malar J* 2020, **19**(1):121.
29. Yobi DM, Kayiba NK, Mvumbi DM, Boreux R, Kabututu PZ, Situakibanza HNT, Umesumbu SE, De Mol P, Speybroeck N, Mvumbi GL *et al*: **Assessment of Plasmodium falciparum anti-malarial drug resistance markers in pfk13-propeller, pfcrt and pfmdr1 genes in isolates from treatment failure patients in Democratic Republic of Congo, 2018-2019**. *Malar J* 2021, **20**(1):144.
30. Yobi DM, Kayiba NK, Mvumbi DM, Boreux R, Kabututu PZ, Akilimali PZ, Situakibanza HNT, De Mol P, Speybroeck N, Mvumbi GL *et al*: **Biennial surveillance of Plasmodium falciparum anti-malarial drug resistance markers in Democratic Republic of Congo, 2017 and 2019**. *BMC Infect Dis* 2022, **22**(1):145.