

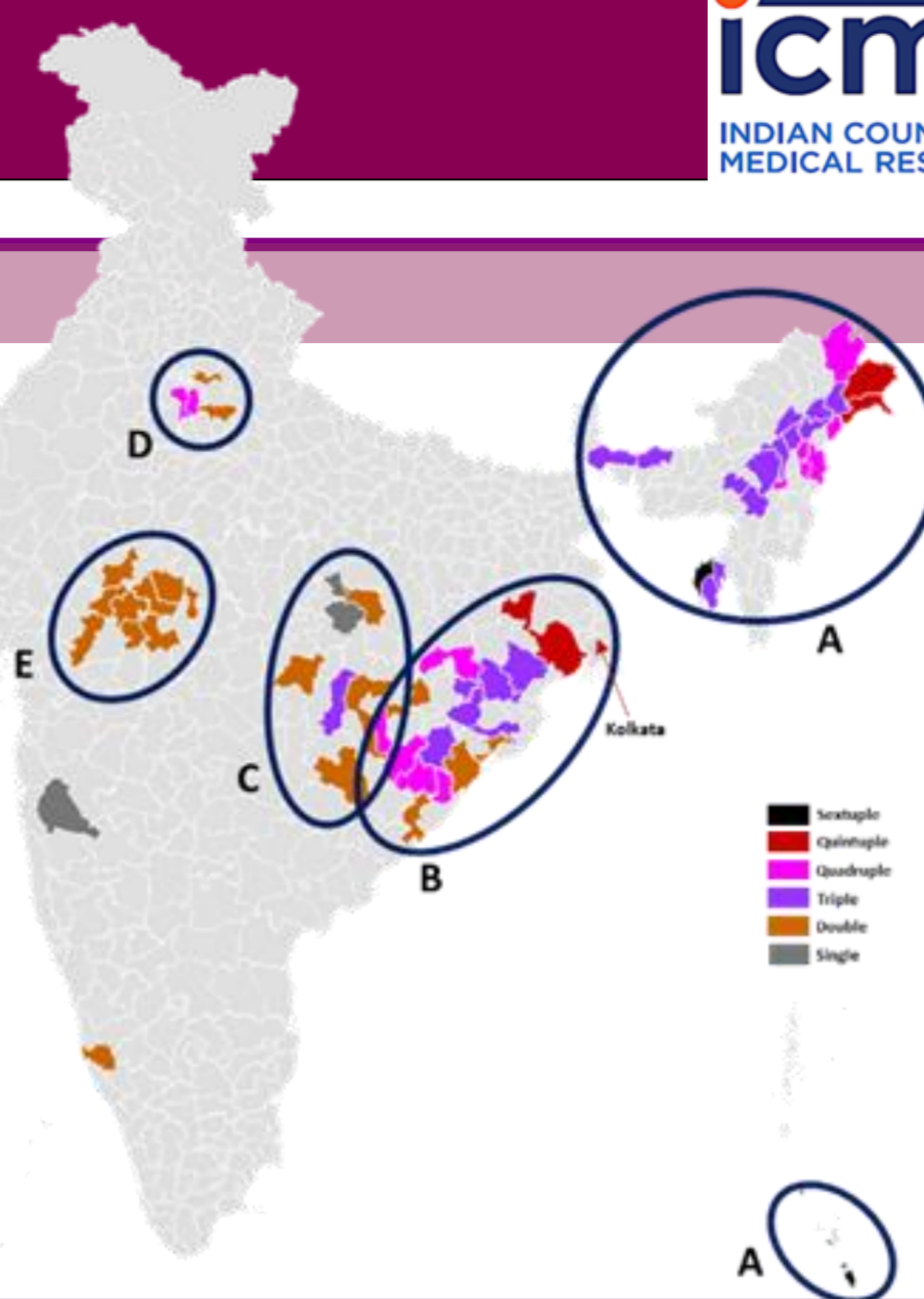
# Meta-analysis on *Plasmodium falciparum* sulfadoxine-pyrimethamine resistance-conferring mutations in India identifies hot spots for genetic surveillance

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## Take home threats!!

- This exhaustive spatiotemporal meta-analysis highlights the need for surveillance of SP-resistance markers in India
- Certain areas (**hot spots**) warrant prioritised molecular surveillance for Pfdhfr (dihydrofolate reductase) & Pfdhps (dihydropteroate synthase) mutations
- The key question is whether there is a need for another antimalarial treatment policy change from AS+SP (artesunate+SP) to AL (artemether+lumefantrine) across India
- The decision needs to be made sooner rather than later



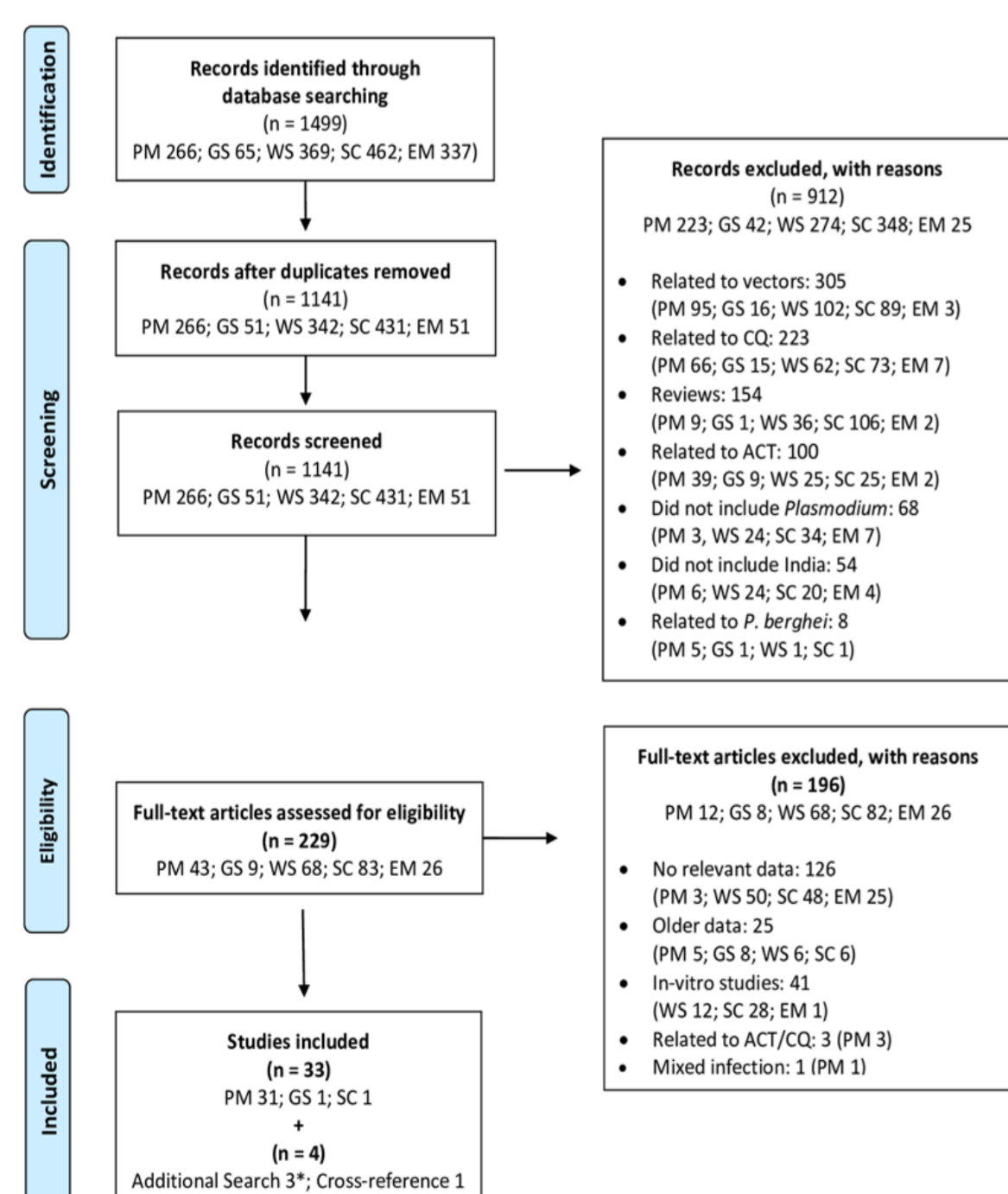
Left: District map of India showing SP resistance marker hot spots (created with <https://gramener.com/map/>). Data encapsulated here are based on the prevalence of Pfdhfr+Pfdhps WHO-validated SP-resistance markers across the country. The criterion for classifying a district as a hot spot for a particular mutation was prevalence of the mutation  $\geq$  lower bound of the 95% CI of the pooled estimate for the country. Hence, the threshold is prevalence  $\geq 4\%$  for single,  $\geq 32\%$  for double,  $\geq 2\%$  for triple,  $>0\%$  for quadruple, and  $\geq 2\%$  for quintuple and sextuple mutations. The hot spot districts are organised into 5 clusters (A-E, from east to west) based on the presence of the mutations conferring the highest order of resistance. Cluster A (sextuple and below), Cluster B (quintuple and below), Cluster C (triple and below), Cluster D (quadruple and below), Cluster E (double)

## Background

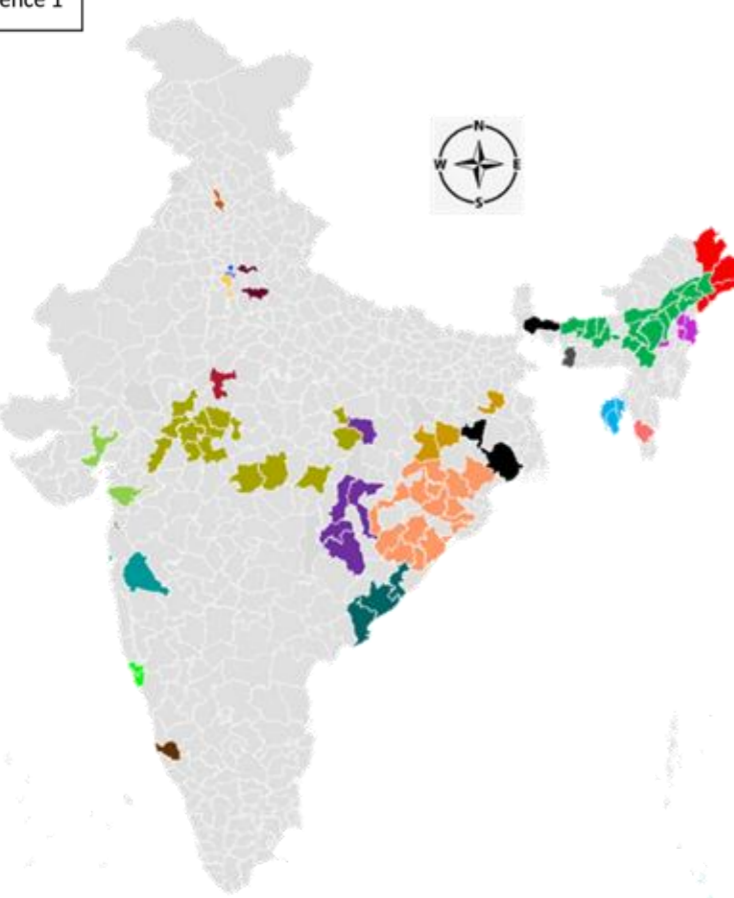
- India is on track to eliminate malaria by 2030 but emerging resistance to first-line antimalarials is a recognised threat
- With delayed parasite clearance by artemisinin, high SP efficacy (and low burden of SP resistance markers) is essential to prevent AS+SP therapeutic failure
- There is a need to systematically monitor the validated mutations in Pfdhfr and Pfdhps genes across India alongside AS+SP therapeutic efficacy studies
- There has been no robust, systematic countrywide surveillance reported for these parameters in India, hence the current study was undertaken

## Approach and Analysis

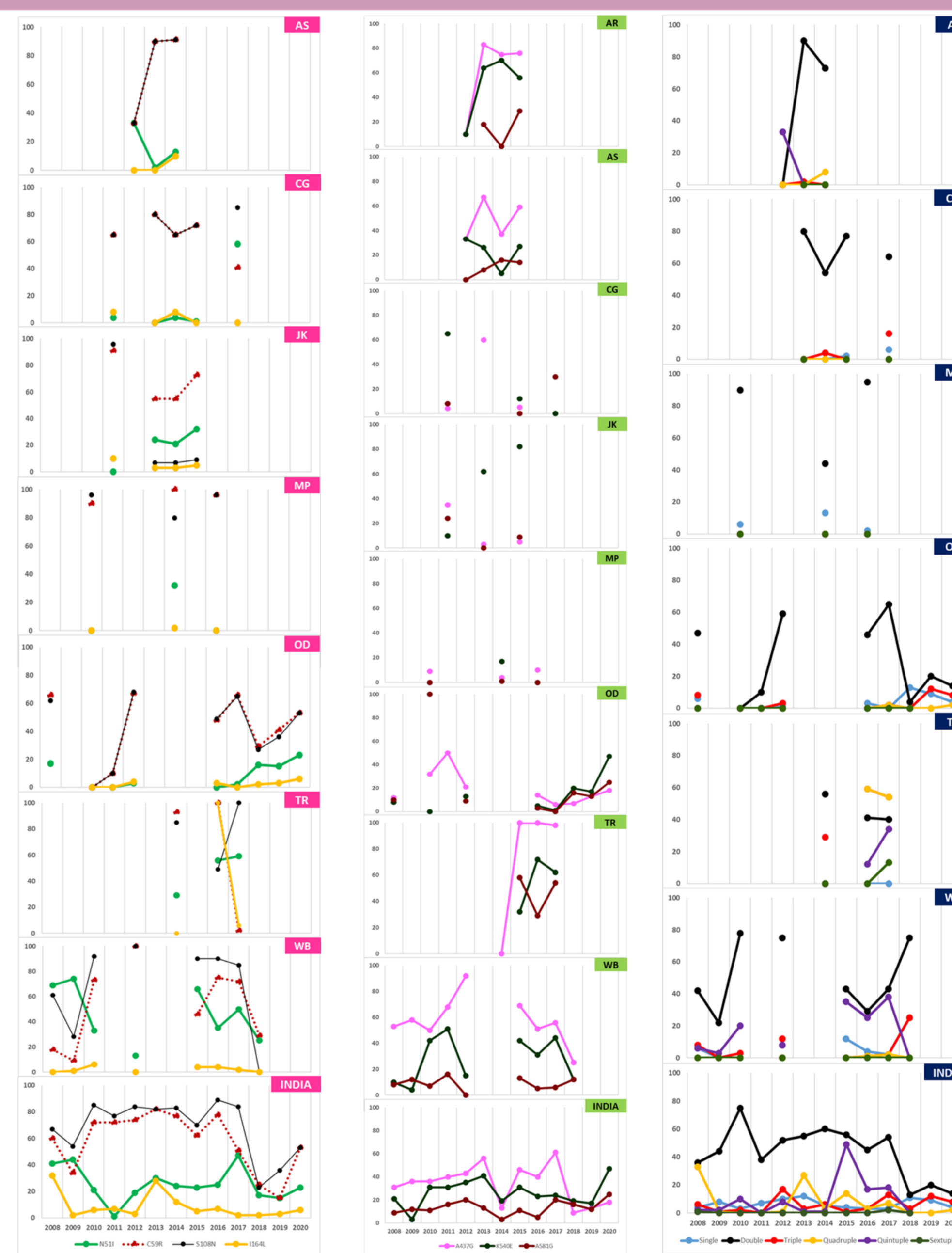
- Studies that reported data on WHO-validated SP resistance markers in *P. falciparum* across India from 2008 to January 2023 were included
- Five major databases (PubMed, Web of Science, Scopus, Embase, and Google Scholar) were exhaustively searched
- Individual and pooled prevalence estimates of mutations were obtained through random- and fixed-effect models
- Data are depicted using forest plots created with a 95% confidence interval and prevalence trends



**Top:** PRISMA flow diagram illustrating the selection of studies for the present systematic review. PM: PubMed Advanced Search Builder; GS: Google Scholar Advanced Search; WS: Web of Science Core Collection Basic Search; SC: Scopus Start Exploring; EM: Embase Quick Search; ACT: Artemisinin-based combination therapy; CQ: Chloroquine.  
**Right:** Data collection sites from various districts in India that were included in this study



## Results



Trends of Pfdhfr (left), Pfdhps (middle) and their combined (right) mutations from 2008-2020. X-axis denotes year of study and Y-axis denotes percentage of mutation. Distribution of Pfdhfr mutation prevalence (%) covered in three or more different years with data breakup are shown. AN: Andaman and Nicobar Islands; AP: Andhra Pradesh; AR: Arunachal Pradesh; AS: Assam; CG: Chhattisgarh; DN: Dadra and Nagar Haveli; GU: Gujarat; GO: Goa; DE: Delhi; HA: Haryana; JK: Jharkhand; KA: Karnataka; MA: Maharashtra; ME: Meghalaya; MI: Mizoram; MP: Madhya Pradesh; NA: Nagaland; OD: Odisha; PU: Punjab; RA: Rajasthan; TR: Tripura; UP: Uttar Pradesh; WB: West Bengal.

