

The WWARN Clinical Trials Publication Library: a live, open-access database of *Plasmodium* treatment efficacy trials



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Background

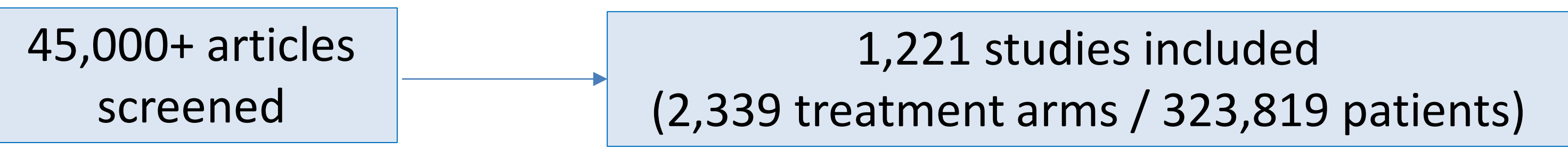
- The rise of antimalarial resistance is threatening malaria control.
- Synthesis of available evidence on antimalarial efficacy is essential for timely and appropriate policy, but labour-intensive and slow.
- Since 2011 WWARN has developed a regularly updated, open-access database of published antimalarial efficacy trials, available to the malaria community as a tool to streamline evidence synthesis.

Methods

Databases searched	PubMed, EMBASE, Web of Science Core Collection, CENTRAL
Time period	Database inception – last search (currently July 2018)
Inclusion criteria	Prospective clinical trials assessing antimalarial efficacy on any <i>Plasmodium</i> species with ≥28 days follow-up
Exclusion criteria	Animal studies, prevention/prophylaxis studies, IPT/IST, MDA, conference abstracts, induced malaria, pooled analyses, severe malaria only

Key variables were extracted into a cloud-based database using REDCap

Results



Descriptive characteristics

- 76% of studies assessed *P. falciparum*, 17% *P. vivax*, 7% both, and 0.4% other species
- 55% were randomised; of this 17% at least single blinded
- 57% included children under 5; 5% included pregnant women
- 2 years median delay from end of participant recruitment to publication (range: <1 year to 13 years)
- 36 studies of imported malaria: mainly *Pv* studies in returning US military or *Pf* in returning European travellers from Sub-Saharan Africa

Temporal trends

- Number of studies published per year increased over time. 70% of *Pf* and 82% of *Pv* studies published after 2000
- Most of this increase due to more studies in Africa, especially for *Pf*

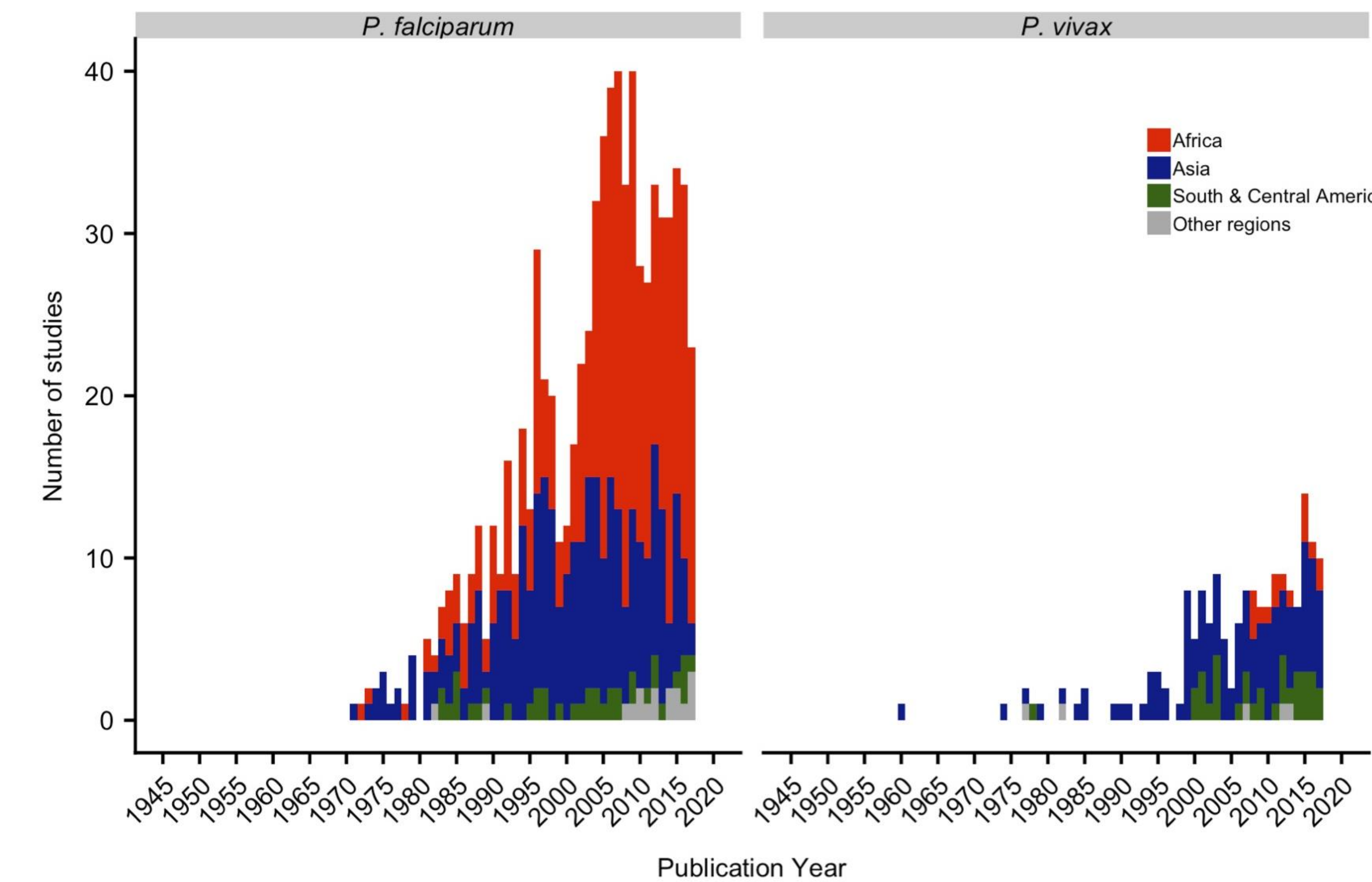


Figure 1. Number of publications per year per region

Results (continued)

Spatial trends

- Majority of studies in Africa (44%) or Asia (44%); 8% in South/Central America. 55 were multi-centre
- Most common centres:
 - Pf*: Thailand (15%), Nigeria (8%), India (6%), Kenya (4%)
 - Pv*: Thailand (19%), India (17%), Brazil (10%), Indonesia (7%)
- In last 5 years, marked increase of studies in African centres for *Pf*

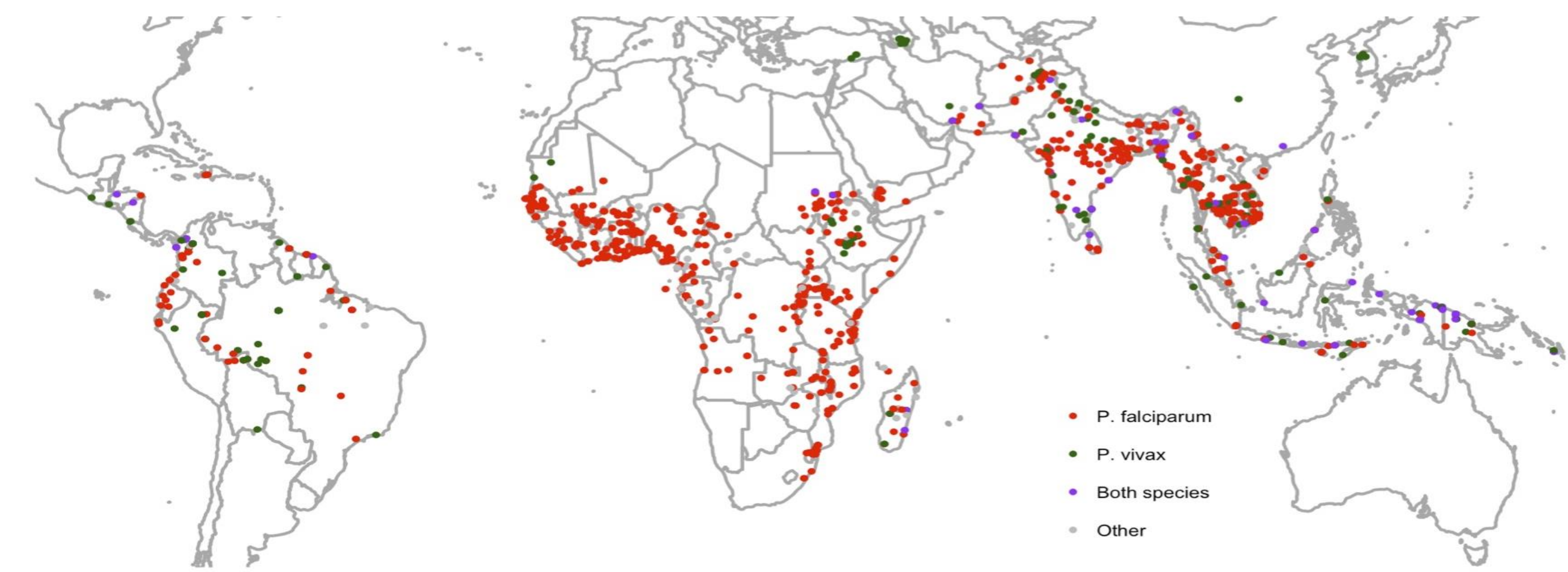


Figure 2. Distribution of study sites

Treatments

- Most common drugs tested:
 - Pf*: artemether-lumefantrine (14% arms / 46,280 patients)
 - Pv*: chloroquine ± primaquine (65% arms / 67,063 patients)
- WHO-recommended ACTs tested in:
 - Pf*: 40% arms overall, 78% in last 5 years
 - Pv*: 11% arms overall, 23% in last 5 years
- Marked increase in *Pf* studies testing ACTs, especially in Africa

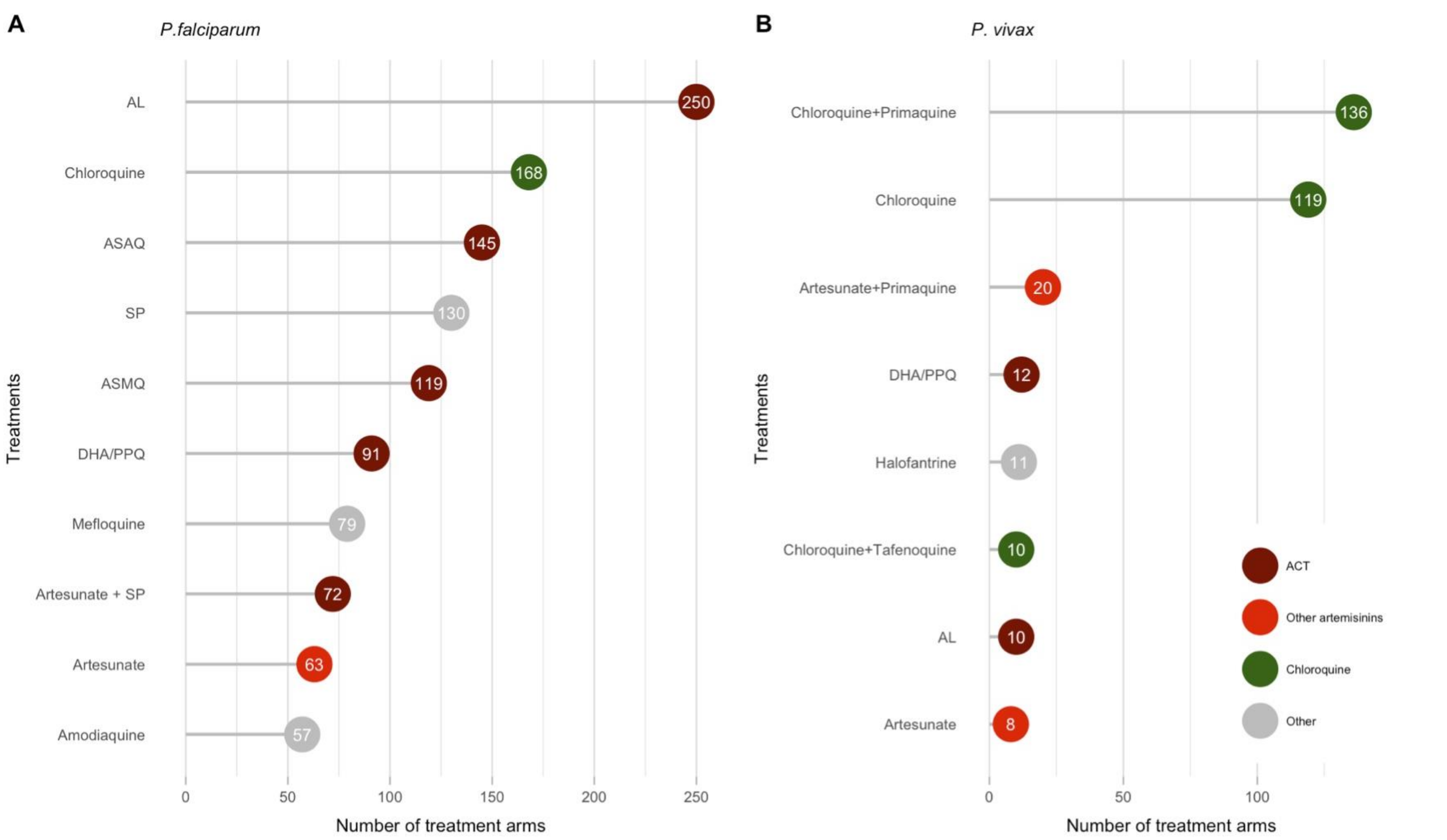


Figure 3. Most common treatment regimens

Conclusions and future work

Changing landscape of antimalarial efficacy trials

- Volume of research on antimalarial therapy increased substantially over 50 years, with a shift from Asia to Africa for *Pf*, and increase in *Pv* studies
- Knowledge gaps remain in some heavily affected countries; non-*Pf* or *Pv* species; and at-risk populations e.g. pregnant women
- Relatively long delay to publication, reflecting the challenge of publishing results that can provide contemporaneous evidence for policymakers

Future perspectives

- The library will be updated every 6 months
- Most recent version available and open-access on the WWARN website
- Represents a novel approach to evidence synthesis/dissemination that can be adapted for other global infectious diseases – currently trialled with other disease themes within the Infectious Diseases Data Observatory (IDDO)