The global burden of *Plasmodium vivax* and G6PD deficiency: updated maps, case estimates & online repositories

APMEN Vivax Working Group
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Rosalind Howes, Katherine Battle, Daniel Pfeffer, Tim Lucas, Dan Weiss, Michele Nguyen, Kate Twohig, Pete Gething.....
Plasmodium vivax maps: prevalence and clinical burden

- Led by Katherine Battle, Tim Lucas, Dan Weiss, Michele Nguyen, Dan Pfeiffer, Kate Twohig, Pete Gething and many others *Paper coming soon

- Objective: *P. vivax* clinical case estimates and high-resolution maps to support sub-national stratification (first *P. vivax* case estimates developed by MAP)

- Part of the Global Burden of Disease effort, now set for annual updates

- Models informed primarily by reported routine clinical case data, but also prevalence surveys and environmental/socio-demographic covariates

- Method applied varies between regions:
  - Outside Africa (+ Djibouti & Eritrea): adjusted case reports downscaled to pixels
  - Within Africa: WMR-reported Pf:Pv ratio applied to the *Pf* results
Methods: outside-Africa (& Djibouti and Eritrea)
Reported case count data

• Data are incomplete: some countries have no subnational data
• Model uses data at all levels simultaneously
• Heterogeneity within polygons is explored with environmental, epidemiological and demographic covariates
Methods: outside-Africa

Reported case data adjustments

• **Treatment-seeking rates** (source: national surveys or gap-filled by model driven by wealth and health infrastructure, education levels, accessibility to care covariates)

• **Reporting completeness** (source: National programmes or World Malaria Report)

• **Diagnostic positivity rate** applied to unconfirmed case counts (source: World Malaria Report)
Input data: 2005

Input Data for Indo-Pacific:
East Timor, Indonesia, Malaysia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu

API (per 1000 population)

0 - 0.1
0
No Data
Consolidated input data: 2005

Input Data for Indo-Pacific:
East Timor, Indonesia, Malaysia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu

API (per 1000 population)

- >600
- 450
- 300
- 150
- 1
- 0.5
- 0.1
- 0
- 0 - 0.1
- No Data
Input data: 2015

Input Data for Indo-Pacific:
East Timor, Indonesia, Malaysia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu

API (per 1000 population)
Consolidated input data: 2015

Input Data for Indo-Pacific:
East Timor, Indonesia, Malaysia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu
Methods: outside-Africa

Time-series of case incidence

- Any gaps are filled using a moving-average model and a range of socio-economic covariates (source: World Bank for national-levels; IHME for sub-national)
- These modelled time series values define the annual national-level case estimates
Methods: outside-Africa
Time-series of case incidence

Indonesia

Myanmar

Thailand
Methods: outside-Africa

Time-series of case incidence

- Cambodia
- Laos
- Papua New Guinea
Methods: outside-Africa
Developing the maps: disaggregation regression model

• Aiming to model the spatial pattern of cases distribution across the polygons to obtain pixel-level annual case incidence maps

• Uses the polygon-level API values from the time series and allocates out cases across the pixels within each polygon by pixel-level suitability
  – Suite of environmental covariates (including PvPR surface) & population surface are at the pixel level
Methods: outside-Africa
Developing the maps: disaggregation regression model

- Model allocates cases on basis of pixel-level suitability, such that they sum to polygon total case counts

Incidence  Population  Pixel Cases  Polygon Cases

Environmental Covariates
Random field
Methods: within Africa (except Djibouti & Eritrea)
Species ratios applied to *P. falciparum* results

- Less complete data on *P. vivax* exists within Africa. Here the methods learn from the data-rich *P. falciparum* predictions.

- Annually reported *Pf:Pv* case ratios as reported by countries to the World Malaria Report are applied to the *Pf* case incidence maps
Pop at Risk & Pv case count estimates, and maps figures are still in development – due for finalisation and publication end 2018/early 2019.
www.map.ox.ac.uk
Now to G6PD...
New literature since 2011

- Pubmed search (April 2018) identified 7,447 new sources, of which n=804 considered likely to include population data.
Updating the G6PDd evidence base

- Explicit objective of the APMEN Vivax Working Group: team effort!

- Updating the maps and population estimates

- Addition of malaria patient surveys

- Creating a centralised online G6PD survey and map repository
Updating the G6PDd evidence base

First pass completed: but gaps in the data

Pubmed literature review

Follow-up with authors to help fill gaps in details

Reach out to experts for unpublished literature

Launch of the G6PD Data Explorer in 2019

September-October 2018

October-December 2018
G6PD Data Explorer

Hosted by the Malaria Atlas Project
Filter

+ Add expression  + Add set

Display features in the layer that match all of the following expressions

DM_TYPE (String)  is  FST

Case sensitive

All of the following expressions in this set are true

AGE (String)  is  newborn

Case sensitive

PERMISSION (String)  is  Yes

Case sensitive

OK  Cancel
G6PDd prevalence surveys (n=89)
Many surveys are missing due to incomplete information
By country
Reported G6PDd prevalence (N>50)
Reported G6PDd prevalence (N>50)
G6PD deficiency variants
Variant occurrence points (n=152)

Many surveys are missing due to incomplete information
Variant occurrence points
Variant surveys: new since 2012
G6PDd prevalence: What should we document & map?

Documenting

- Community-based representative surveys
- Malaria-patient surveys
- Demographics: ethnicity, age, gender
- Survey location
- Diagnostic details

Mapping/population estimates

- Male G6PDd prevalence: ~30% threshold of the adjusted male median
- Female homozygous and heterozygous frequencies by assuming Hardy-Weinberg equilibrium
- Previously derived female counts at ~30% threshold (as per available diagnostics), but not consistent with current risk assessments

Healthy & malaria patient groups
G6PDd variants: What should we document & map?

Documenting
- Polymorphic and phenotypically significant mutations
- Avoiding duplication of gene sequence repositories

Mapping
- Previously: pie charts of relative proportions among G6PDd individuals (< ~30% activity)
- Increasing tendency towards population allele frequencies (without prior screening)
Thank you

- APMEN Vivax Working Group:
  - All the data contributors: NMCPs & researchers

- MAP team, in particular:
  - *P. vivax*: Katherine Battle, Tim Lucas, Dan Weiss, Michele Nguyen, Kate Twohig, Daniel Pfeffer, Pete Gething & many others
  - G6PD data updates: Daniel Pfeffer, Colin Johnston, Jonas Sandbrink, Jia Wei
  - Online data explorers: Jen Rozier, Joe Harris, Harry Gibson, Mike Thorn