Analysis-ready datasets for insecticide resistance phenotype and genotype frequency in African malaria vectors

Catherine L. Moyes1, Antoinette Wiebe1, Katherine Gleave2, Anna Trett2, Penelope A. Hancock3, Germain Gil Padonou3, Mouhamadou S. Chouaïbou4, Arthur Sovi5,6, Sara A. Abuelmaali6, Eric Ochomo7, Christophe Antonio-Nkondjo8, Dereje Dengela9, Hitoshi Kawada10, Roch K. Dabire11, Martin J. Donnelly2, Charles Mbogo12,13, Christen Fornadel14 & Michael Coleman2

The impact of insecticide resistance in malaria vectors is poorly understood and quantified. Here a series of geospatial datasets for insecticide resistance in malaria vectors are provided, so that trends in resistance in time and space can be quantified, and the impact of resistance found in wild populations on malaria transmission in Africa can be assessed. Specifically, data have been collated and geopositioned for the prevalence of insecticide resistance, as measured by standard bioassays, in representative samples of individual species or species complexes. Data are provided for the Anopheles gambiae species complex, the Anopheles funestus subgroup, and for nine individual vector species. Data are also given for common genetic markers of resistance to support analyses of whether these markers can improve the ability to monitor resistance in low resource settings. Allele frequencies for known resistance-associated markers in the Voltage-gated sodium channel (Vgsc) are provided. In total, eight analysis-ready, standardised, geopositioned datasets encompassing over 20,000 African mosquito collections between 1957 and 2017 are released.

Background & Summary

Current malaria control activities are heavily reliant on vector control using insecticides, which means resistance to these compounds has the potential to derail control efforts1–5. Studies have started to investigate the impact of resistance in certain situations6–8 but a full understanding of impact requires comprehensive quantification of resistance. To quantify the factors that influence vector control generally, data from vector populations are required and a number of vector databases are already available for species distributions, infection prevalence, and bionomic parameters5–12. A database for insecticide resistance in malaria vectors, that allows users to

1Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, University of Oxford, Oxford, OX1 7LF, UK. 2Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool L1, UK. 3Centre de Recherche Entomologique de Cotonou (CREC), 06BP2604, Cotonou, Benin. 4Centre Suisse de Recherches Scientifiques en Côte d’Ivoire, 01BP1303, Abj 01, Abidjan, Côte d’Ivoire. 5Faculty of Agronomy, University of Parakou, BP123, Parakou, Benin. 6Department of Medical Entomology, National Public Health Laboratory, Federal Ministry of Health, Khartoum, Sudan. 7Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya. 8Laboratoire de Recherche sur le Paludisme, Organisation de Coordination pour la lutte Contre les Endémies en Afrique Centrale (OCEAC), P.O. Box 288, Yaoundé, Cameroon. 9U.S. PMI VectorLink Project, Abt Associates, 6130 Executive Boulevard, Rockville, MD, 20852, USA. 10Department of Vector Ecology and Environment, Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan. 11Department of Medical Biology and Public Health, Institut de Recherche en Science de la Santé, Bobo-Dioulasso, Burkina Faso. 12KEMRI Centre for Geographic Medicine Research-Coast, P.O. Box 230-80108, Kilifi, Kenya. 13KEMRI-Wellcome Trust Research Program, P.O Box 43640-00100, Nairobi, Kenya. 14US President’s Malaria Initiative, US Agency for International Development, Washington, DC, USA.

Correspondence and requests for materials should be addressed to C.L.M. (email: catherinemoyes@gmail.com)
download analysis-ready datasets, it is vital so that the impact of levels of resistance found in wild populations, on malaria transmission, can be assessed. These datasets are also essential to quantify trends in resistance in space and time, filling the gaps in the available data with robust predictions, to aid resistance management and the deployment of interventions designed to counter resistance.

Studies of phenotypes in natural populations may be confounded by variation in the environments sampled, including factors linked to climate, land use and malaria control interventions. It is not possible to control for all variables in the natural environment but this issue can, in part, be mitigated by sampling a large number of locations encompassing different combinations of environmental variables. Large, collated datasets do, however, have potential disadvantages. Collated datasets that are a combination of data points representing different types of sample, different measurement methods, different location types and so on, risk undermining any analysis that is performed.

Each dataset should be constructed to address a specific question or set of questions, and the data within each set needs to be standardised to allow robust analyses. The goal of the current work was to collate data from multiple studies characterising the insecticide resistance phenotype and genotype in communities of malaria vectors at as many locations and times as possible. The first aim was then to generate standardised datasets designed to address specific questions using geospatial analyses. Namely, what are the trends in resistance in time and space in specific vector assemblages, to then assess whether these trends are associated with trends in malaria transmission. The second aim was to provide data that can be used to investigate associations between genetic markers for individual mechanisms of resistance and the insecticide resistance phenotype, to assess whether genetic markers can improve the ability to monitor resistance in low resource settings.

Methods

Data sources. Data were obtained from published journal articles, published reports, and unpublished datasets. Published journal articles were identified in the Web of Science bibliographic database by using the search terms “insecticide resistance” and “anopheline” together with the name of each malaria endemic country in turn. The Web of Science was chosen because it incorporates many relevant databases including the SciELO Citation Index from 1997 onwards, MEDLINE from 1950 onwards (from the U.S. Library of Medicine), the Data Citation Index from 1993 onwards (provides details of datasets in international data depositories), the BIOSIS Citation Index from 1969 onwards (covers pre-clinical, experimental, and animal research) and the Web of Science’s own Core Collection from 1945 to date.

The earliest date was unrestricted, and the search was completed on 31 December 2017. The initial search yielded 3,685 articles published from 1956 to 2017, with the first African paper published in 1957. Data were extracted from each article as outlined below and 342 articles provided data from field samples of mosquitoes collected in malaria endemic African countries for either the insecticide resistance phenotype and/or genotype. If values for some data fields were missing, the authors were contacted. In these instances, either (i) the phenotype/genotype data was given in the article but supplementary information such as the date of sampling or mosquito identification method was missing, or (ii) the genotype/phenotype data were missing, or had been aggregated across sites or years, so the disaggregated data for each site-year were requested. In the latter instance, any genotype/phenotype data received from the authors were treated as unpublished. In total, 81 sets of authors were contacted about 114 journal articles. Of these, 56 sets of authors provided further information; 30 sets of authors confirmed details such as the collection dates and 26 sets of authors provided test results that were not published with the original articles, as well as confirming any missing details of their study.

In addition, agencies reporting on vector surveillance and groups involved in large studies that had not yet published their results, were asked to provide these reports and unpublished datasets. In total, 48 reports and unpublished datasets from African countries were provided. For all unpublished data, permission to include these data in this release was requested. Of a total of 11,057 unpublished data points, permission was received to release 10,834.

Data aggregation/disaggregation. The aim of this work was to provide measures of insecticide resistance for representative samples of a species population (or a species complex or a subgroup) found at a particular time and place, rather than data at the level of an individual mosquito. Replicates from the same mosquito collection sampled at a single “site” and “collection period” were aggregated. The spatial resolution of a “site” was defined by the original field studies and classified by the current study, as described in the data geo-referencing section below. The temporal resolution of a “collection period” was also defined by the original data generators and the duration of each collection period was recorded in the current dataset, as described below. If the reported data had been pooled across multiple sites or collection periods, but was originally obtained at a finer resolution, the disaggregated data for each site-period were requested. For example, if mosquitoes were collected from five sites and bioassayed separately, giving a bioassay result for each site, but only a single average result for the region was published, then the five separate results were requested. The purpose of this disaggregation was to avoid imprecise estimates associated with large areas or long time periods wherever possible. Further details on appropriate methods to analyse data at different resolutions is given in the Usage Notes.

Datasets were constructed based on mosquito samples that represented either a single species or a species complex or subgroup. Species-level data were entered wherever it was available and aggregated to provide data for the species complex later, using the original species composition. If insecticide resistance data were provided for each species but the original species composition was not available for that study, the data points for each individual species were included in the species-level datasets (provided they met the inclusion criteria below) but they were not aggregated to provide data for the species complex. Data are provided for individual species within the An. gambiae complex (An. arabiensis, An. coluzzii, An. gambiae, An. melas and An. quadriannulatus) and for species within the An. funestus subgroup (An. funestus and An. parensis) within datasets 2, 7 and 8. Separately,
Data for individual species were obtained from studies that either sorted egg batches based on mothers’ species or F1 generation from a field collection of An. funestus or F1 generation from a field collection of An. gambiae (Table 1). The mortality for the field sample, this corrected mortality value was entered in the database.

Inclusion criteria for data extraction. Subgroup-, complex- or species-level insecticide resistance phenotype data generated from either a WHO susceptibility test16–26 or a CDC bottle bioassay27 using either the F0 or F1 generation from a field collection of Anopheles mosquitoes were included (Supplementary Information).

Susceptibility tests use two types of control; for the first control, a known susceptible mosquito strain is exposed to the insecticide-treated paper to test that the paper is working, and for the second control, a subsample of the mosquito population being tested are not exposed to the insecticide to check the baseline mortality rate. Data were excluded if the susceptible strain control failed, i.e. mortality in the susceptible strain was <100% indicating that the insecticide-treated paper was not effective. If the first control was successful (all of the mosquitoes died) and a baseline mortality rate was obtained from the second control and used in Abbot’s formula to correct the mortality for the field sample, this corrected mortality value was entered in the database.

Subgroup-, complex- or species-level data on the resistance variants in the voltage-gated sodium channel (Vgsc) gene that were derived from F0 or F1 generations from field collections of Anopheles mosquitoes, provided as either genotype or allele frequencies, were included. Only mosquito samples that were representative of a species complex or subgroup and/or a species were included and any samples that were subject to sub-setting that biased the original sample were excluded. For example, if a mixed species sample was collected but a bioassay result was only reported for the most common species, that bioassay result cannot be considered as representative of the species complex at that time and place. In this example, the data were included in the species-level datasets released here, but these values were not included in the datasets for species complexes. Similarly, if a mixed species sample was collected and then the F1 generation was sorted into single species by identifying the mother of each egg batch, those results cannot be considered representative of the species complex at that time and place. Furthermore, if the allele frequency was calculated for mosquitoes that survived a bioassay, and dead mosquitoes were not tested, this result cannot be considered representative for either the species complex, or the individual species, and was not included in any dataset. If a mixture of dead and alive mosquitoes from a bioassay were tested to obtain an allele frequency, but the ratio of dead:alive was not representative of the original sample, for example 80% died in the bioassay but the sample tested was 50:50 then these data were also excluded.

Individual data files. The full database was used to generate eight individual data files (Table 1) that address specific questions for defined sets of mosquitoes.

The aim in creating Data Files 1 and 2 was to provide a set of comparable results for each insecticide from bioassays that had used the same insecticide concentration and exposure duration, however, the recommended concentrations and durations vary with WHO protocol versions18–26. The protocol version used to define the standard insecticide concentrations and exposure durations in Data Files 1 and 2 was the 1998 WHO test procedures, because the highest volumes of data across all years were available for the concentrations and durations specified by this protocol version26. Insecticides that were not covered by the 1998 protocol version were specified in the 2013 version so this later protocol was also used to set the standard values for Data Files 1 and 226.

Data fields. The data fields included in this release are described in Tables 2–7. The source data fields (Table 2), the sample collection data fields (Table 3), and the geo-location data fields (Table 4) are provided in all data files. The species identification data fields (Table 5) are provided in Data Files 2, 4, 7 and 8. The bioassay data fields (Table 6) are provided in Data Files 1–5. The Vgsc data fields (Table 7) are provided in Data Files 6–8.

All of the data fields were extracted and entered as they were provided by the data source. If any information was missing, no value was entered (see the missing data section below) and the authors were contacted. The only values that were generated after the data were extracted from the sources, were the geo-location values. Full details on how the geo-location data were generated is given in the next section.

Data files are provided for species complexes or subgroups, and for individual species, separately. Bioassay data for individual species were obtained from studies that either sorted egg batches based on mothers’ species prior to a bioassay being performed, or disaggregated the results by species after the bioassay was performed.

| Number | Title | No. data points |
|--------|-------|-----------------|
| 1      | Standard WHO susceptibility test results for the Anopheles gambiae complex and Anopheles funestus subgroup. | 13,618 |
| 2      | Standard WHO susceptibility test results for individual species. | 3,525 |
| 3      | Standard CDC bottle bioassay results for the Anopheles gambiae complex and An. funestus subgroup. | 1,061 |
| 4      | Paired WHO susceptibility test or CDC bottle bioassay results with and without a synergist (An. gambiae complex and An. funestus subgroup). | 1,013 |
| 5      | WHO and CDC intensity bioassay results (An. gambiae complex and An. funestus subgroup). | 1,816 |
| 6      | Vgsc allele frequencies for the An. gambiae complex and An. funestus subgroup. | 1,068 |
| 7      | Vgsc allele frequencies for individual species. | 1,890 |
| 8      | Paired Vgsc allele frequencies from dead and alive subsamples after an insecticide susceptibility test. | 296 |

Table 1. Summary of each of the eight data files released.
or instances where all mosquitoes in the original sample were found to be one species after the bioassay was performed.

For Data File 4, an additional identifier (the “matched set ID”) is included to allow results from bioassays that used the same mosquito collection and exactly the same bioassay conditions, with or without a synergist, to be identified. The same approach was used for Data File 5 where the “matched set ID” allows results from bioassays that used the same mosquito collection and exactly the same bioassay conditions, but with differing insecticide concentrations and/or exposure durations, to be identified. In total, 453 matched sets are provided in the synergist dataset, 463 in the intensity assay data file, and 148 for \( V_{gsc} \) allele frequencies in paired dead and alive subsamples.

**Data geo-referencing.** In order to use these data in geospatial models at a resolution of \( \sim 5 \) km, each mosquito collection location was classed as either a point (defined as a site located within a 2.5 arc-minute grid cell, i.e. an area of \( \sim 5 \times 5 \) km) or a polygon (defined as a site with an area greater than that of a point).

To determine whether a site should be classified as a point or a polygon, we used all information provided by the data source. This included text describing the site, the site name, and any maps or coordinates provided. If the text described the site as a district, or similar, then we checked that the area of that district matched our definition of a polygon and, if so, used the polygon classification. If coordinates were provided that mapped to the centroid of an administrative unit then we checked whether the site name and text description matched that administrative unit and, if so, classified the site as a polygon (unless the area of the administrative unit was less than \( 5 \times 5 \) km).

For all sites defined as ‘points’ the following steps were followed. The site name and all contextual information about the location of the site were noted, for example, the district the site was in, its proximity to a major city.
or other geographical features, and so on. If the data source provided coordinates, then these were converted to decimal degrees. If no coordinates were provided, the site name was searched in at least two online gazetteers (Google Maps, GeoNames, OpenStreetMap, WikiMapia and so on). All options identified by this search were cross-checked against the contextual information. If only one option matched the contextual information, or more than one option matched the contextual information, or no options were found that matched the contextual information, the individuals who published or provided the data were contacted. For all possible coordinates were obtained for a study, they were plotted on a map to ensure the data spread for that study matched any information available on the authors’ overarching sampling strategy.

For all sites defined as ‘polygons’, any contextual information was noted, such as the province that the district was in. The name of the area in question was searched in the FAO’s Global Administrative Unit Layers (GAUL, http://www.fao.org/geonetwork/srv/en/metadata), using fuzzy matching to allow for different spellings or transliteration, and checked against any available contextual information. If a single administrative unit in GAUL matched the area name and contextual information, the GAUL code (=a unique identifier for that area/polygon),

### Table 6. WHO and CDC bioassay data fields. There data fields are included in Data Files 1–5.

| Title                              | Data type   | Description                                                                 |
|------------------------------------|-------------|-----------------------------------------------------------------------------|
| Species                            | Category    | The species that the bioassay result represents.                            |
| Complex/subgroup                   | Category    | The species complex or subgroup that the bioassay result represents.         |
| Generation                         | Category    | The mosquito generation tested: F0, F1 or a mix of both.                    |
| Test protocol                      | Category    | The WHO or CDC bioassay protocol followed is listed.                        |
| Insecticide                        | Category    | The insecticide tested is named.                                            |
| Concentration (%)                  | Decimal     | If a WHO protocol was followed, the insecticide concentration is given as a percent. |
| Concentration (µg/bottle)          | Decimal     | If the CDC protocol was followed, the insecticide concentration is given in µg/bottle. |
| Exposure period (minutes)          | Integer     | The period of exposure to the insecticide in minutes.                       |
| No. mosquitoes tested              | Integer     | The total number of mosquitoes tested in all replicates.                    |
| No. mosquitoes dead                | Integer     | The total number of mosquitoes that died in all replicates.                 |
| Percent mortality                  | Decimal     | The percent of mosquitoes that died across all replicates, adjusted using Abbott's formula if applicable. |

### Table 7. Vgsc gene data fields. These data fields are included in Datasets 6–8.

| Title                              | Data type   | Description                                                                 |
|------------------------------------|-------------|-----------------------------------------------------------------------------|
| Species                            | Category    | The species that the bioassay result represents.                            |
| Complex/subgroup                   | Category    | The species complex or subgroup that the bioassay result represents.         |
| Generation                         | Category    | The mosquito generation tested: F0, F1 or a mix of both.                    |
| Test protocol                      | Category    | The WHO or CDC bioassay protocol followed is listed.                        |
| Insecticide                        | Category    | The insecticide tested is named.                                            |
| Concentration (%)                  | Decimal     | If a WHO protocol was followed, the insecticide concentration is given as a percent. |
| Concentration (µg/bottle)          | Decimal     | If the CDC protocol was followed, the insecticide concentration is given in µg/bottle. |
| Exposure period (minutes)          | Integer     | The period of exposure to the insecticide in minutes.                       |
| No. mosquitoes tested              | Integer     | The total number of mosquitoes tested in all replicates.                    |
| No. mosquitoes dead                | Integer     | The total number of mosquitoes that died in all replicates.                 |
| Percent mortality                  | Decimal     | The percent of mosquitoes that died across all replicates, adjusted using Abbott's formula if applicable. |

or other geographical features, and so on. If the data source provided coordinates, then these were converted to decimal degrees. If no coordinates were provided, the site name was searched in at least two online gazetteers (Google Maps, GeoNames, OpenStreetMap, WikiMapia and so on). All options identified by this search were cross-checked against the contextual information. If only one option matched the contextual information, the coordinates were extracted from the online gazetteer and added to the database. If more than one option matched the contextual information, or no options were found that matched the contextual information, the individuals who published or provided the data were contacted. In these instances, no coordinates were entered without external confirmation. After all possible coordinates were obtained for a study, they were plotted on a map to ensure the data spread for that study matched any information available on the authors’ overarching sampling strategy.

For all sites defined as ‘polygons’, any contextual information was noted, such as the province that the district was in. The name of the area in question was searched in the FAO’s Global Administrative Unit Layers (GAUL, http://www.fao.org/geonetwork/srv/en/metadata), using fuzzy matching to allow for different spellings or transliteration, and checked against any available contextual information. If a single administrative unit in GAUL matched the area name and contextual information, the GAUL code (=a unique identifier for that area/polygon),
and administrative level for that unit, were extracted and entered in the database. If an administrative unit within GAUL could not be identified, no code was entered.

If an individual site could not be located, or could not be precisely located within a 2.5 arc-minute grid cell, then the data point was linked to the second order administrative division that the site falls within. The administrative division was identified using the same method as for polygons above.

If multiple point locations were sampled and the mosquitoes were pooled before being tested (or only the pooled results were available), the site type was classified as a ‘multi-point’ and the coordinates for all of the individual point locations were linked to the test result.

Missing data. If data for a particular field was missing from the original data source, the value was recorded as NR, i.e. not reported. For values that were not applicable, rather than missing, NA was used. For example, if only one capture method was used, the value entered for the second capture method was NA. If the geographical coordinates for a site could not be identified (see above), NF was entered, i.e. not found.

If a study did not explicitly state the insecticide concentration, exposure period and/or minimum number of mosquitoes used, but did specify the protocol followed, it may be possible to obtain the missing information from the relevant protocol. Protocol values for the most commonly used insecticides are provided in Tables 8 and 9, and the values for all insecticides are given in the Supplementary Information, to allow data users to fill these data gaps if they wish.

| Protocol | Min. no. mosquitoes | Duration (minutes)a | Duration for fenitrothion (minutes) | Duration for DDT (minutes) |
|----------|---------------------|---------------------|-------------------------------------|---------------------------|
| WHO 1963 | 60                  | 60                  | 60                                  | 60                        |
| WHO 1970 | 60                  | 60                  | 60                                  | 60                        |
| WHO 1975 | 60                  | 60                  | 60                                  | 60                        |
| WHO 1976 | 60                  | 60                  | 60                                  | 60                        |
| WHO 1980 | 60                  | 60                  | 120                                 | 60                        |
| WHO 1981 | 60                  | 60                  | 120                                 | 60                        |
| WHO 1986 | 60                  | 60                  | 120                                 | 60                        |
| WHO 1992 | 60                  | 60                  | 120                                 | 60                        |
| WHO 1998 | 80                  | 60                  | 120                                 | 60                        |
| WHO 2013 | 80                  | 60                  | 120                                 | 60                        |
| WHO 2016 | 80                  | 60                  | 120                                 | 60                        |
| CDC bottle bioassay | 100 | 30 | 30 | 45 |

Table 8. Minimum recommended number of mosquitoes and duration of exposure specified by published protocols for the WHO susceptibility test and CDC bottle bioassay. The exposure duration values from the WHO protocols apply to dieldrin, malathion, fenthion, propoxur, chlorphoxim, permethrin, deltamethrin, λ-cyhalothrin, bendiocarb, etofenprox, pirimiphos-methyl, carbosulfan, cyfluthrin, chlorfenapyr, fipronil and α-cypermethrin. The CDC protocol values apply to bendiocarb, cyfluthrin, cypermethrin, deltamethrin, fenitrothion, λ-cyhalothrin, malathion, permethrin and pirimiphos-methyl. Full details can be found in the published protocols.

| Protocol | DDT | deltamethrin | permethrin | bendiocarb | λ-cyhalothrin | primiphos-methyl |
|----------|-----|--------------|------------|------------|---------------|-----------------|
| WHO 1963 | M.C. |              |            |            |               |                 |
| WHO 1970 | M.C. |              |            |            |               |                 |
| WHO 1975 | M.C. |              |            |            |               |                 |
| WHO 1976 | M.C. |              |            |            |               |                 |
| WHO 1980 | 4%  | 0.025%       | 0.25%      |            |               |                 |
| WHO 1981 | 4%  | 0.025%       | 0.25%      | 0.1%       |               |                 |
| WHO 1986 | 4%  | 0.025%       | 0.25%      |            | 0.1%          | 0.05%           |
| WHO 1992 | 4%  | 0.025%       | 0.25%      | 0.1%       | 0.1%          |                 |
| WHO 1998 | 4%  | 0.05%        | 0.75%      | 0.1%       | 0.1%          | 0.05%           |
| WHO 2013 | 4%  | 0.05%        | 0.75%      | 0.1%       | 0.05%         | 0.25%           |
| WHO 2016 | 4%  | 0.05%        | 0.75%      |            | 0.05%         | 0.25%           |
| CDC bottle bioassay | 100µg/bottle | 12.5 µg/bottle | 21.5 µg/bottle | 12.5 µg/bottle | 12.5 µg/bottle | 20 µg/bottle |

Table 9. Insecticide concentrations specified by published protocols for the WHO susceptibility test and CDC bottle bioassay. M.C. denotes that multiple concentrations were recommended so the actual concentration used in any particular bioassay cannot be inferred from the protocol version.
Data duplication. The data extracted came from several hundred different sources, which introduced the possibility that individual results had been entered into the database more than once. To identify duplicates the following data fields were used: original sample; species tested; date fields; no. mosquitoes tested; no. mosquitoes dead; percent mortality; site name; coordinates. Fuzzy matching was used for all fields to identify duplicates where different levels of aggregation had been used, or different data values were missing, or names were spelled differently. All partial matches were examined to identify genuine duplicates. Duplicate data points were removed, and the source details linked to the single data point that was retained. In total, 3,483 duplicated data points were removed. The final lists of species and insecticides that were included are given in Tables 10 and 11.

Data Records. The data are available for download from the Dryad Digital Repository. The spatial and temporal distributions of Data File 1, standard WHO susceptibility test results for the Anopheles gambiae complex and Anopheles funestus subgroup, are shown in Fig. 1. The spatial and temporal distributions of Data File 7, Vgsc allele frequencies for individual species, are shown in Fig. 2.

Data File 1 is the largest dataset but all eight have similar spatial distributions with clustered sampling in the east and west of Africa and sparse data points in the centre and southwest. They also share similar temporal distributions with phenotypic data volumes increasing throughout the time period particularly from 2008 onwards, and the genotypic data volumes peaking in 2005 and 2010. The genotype data were almost exclusively extracted from published papers and there is typically a lag of around two years between mosquito collection and the publication of a paper containing the test results.

In addition to the data extracted for Vgsc allele frequencies, data were also identified for Ace-1 allele frequencies and metabolic mechanisms of resistance including cytochrome P450s, esterases and glutathione-S-transferases. The volumes of genetic and biochemical data currently available for these mechanisms of resistance did not meet

| Species, complexes and subgroups tested | Complex/subgroup |
|----------------------------------------|------------------|
| An. arabiensis                          | An. gambiae complex |
| An. coluzzii                            | An. gambiae complex |
| An. gambiae                             | An. gambiae complex |
| An. melas                               | An. gambiae complex |
| An. quadriannulatus                     | An. gambiae complex |
| An. gambiae complex                     | not applicable |
| An. funestus                            | An. funestus subgroup |
| An. parensis                            | An. funestus subgroup |
| An. funestus subgroup                   | not applicable |
| An. rivulorum                           | An. funestus group |
| An. gambiae complex not applicable      |                  |
| An. funestus subgroup not applicable    |                  |

Table 10. List of the species, complexes and subgroups that were tested and are included in the datasets for release.

| Insecticides tested |
|---------------------|
| α-cypermethrin      |
| bendiocarb          |
| carbosulfan         |
| chlorpyrifos-methyl |
| cyfluthrin          |
| DDT                 |
| deltamethrin        |
| dieldrin            |
| etofenprox          |
| fenitrothion        |
| fenthion            |
| λ-cyhalothrin       |
| malathion           |
| permethrin          |
| pirimiphos-methyl   |
| propoxur            |

Table 11. List of the insecticides that were tested and are included in the datasets for release.
our aim of providing standardised data for a large number of locations across Africa, so no collated datasets for these mechanisms were generated. Dataset 4 consists of results from synergist bioassays so it does, therefore, provide data linked to P450-mediated mechanisms of resistance.

Many studies performed both bioassays and genetic tests. If links between the different tests performed on the same sample of mosquitoes were provided by the original study, and providing any subsamples tested were not biased, then it was possible to extract pairs of phenotypic and genotypic measures of resistance for samples from a specific time and place. Unfortunately, however, when instances of paired phenotypic and genotypic results for an individual species from a single time and place were extracted, only sixty pairs were identified. This volume of data did not meet our aim of providing standardised data for a large number of locations across Africa. The same was true for paired phenotypic and genotypic results for a species complex or subgroup from a single time and place.

In addition, the data volumes available for species-level CDC bottle bioassay results, species-level paired bioassays with and without a synergist, and species-level intensity bioassays, were too low to meet our aim of providing standardised data for a large number of locations across Africa.

**Technical Validation**

Data were checked for internal consistency to ensure (i) all coordinates for point locations fell on land and in the right country, as defined by GADM, (ii) mortality and allele frequencies never exceeded 100%, (iii) the collection end date was never earlier than the collection start date, and (iv) the species name tallied with the identification methods listed. A matrix of species identification methods and species identified by each method was prepared in order to complete this check (Supplementary Information). In addition, a second person reviewed the geographical coordinates in accordance with the geo-locations protocol outlined above.
Usage Notes

Each data file released has been designed to provide results for a representative sample of a species complex or subgroup, or an individual species, so users can be confident of what each set of results represents. Older versions of the collated datasets of WHO susceptibility test results and the $V_{gsc}$ allele frequency have been used in a prior geostatistical analysis that aimed to identify associations among resistance to different insecticides in the An. gambiae species complex. The data files have been designed for use in geospatial analyses and, in such analyses, the precise location for each data point is important for two reasons. First, because this allows accurate calculation of the Euclidian distances between points for analyses that exploit spatial correlations in the data. Secondly, precise location information allows accurate matching of the data to a wide range of environmental variables, such as climatic, socio-economic and intervention variables, to exploit relationships between the biological data and these environmental variables. The use of data linked to wider areas is a current area of research aimed at improving model predictions in circumstances where data linked to precise locations are particularly sparse. For any kind of spatial analysis, it is essential to know whether the geographical coordinates provided represent a precise location or wider area, what the definition of a precise location is, and where the boundaries of the wider areas lie. The data points released here are linked to a mixture of precise locations and wider areas, the precise locations (referred to here as points) are defined as an area within a 2.5 arc-minute grid cell (approx. $5 \times 5$ km), and links to the boundaries of wider areas (referred to here as polygons) are given.

The data files released here are not the result of one single, continent-wide study that used a standard sampling design. It is a compilation of many studies that used many designs and incorporates obvious sampling bias. Sites that are more easily accessed or closer to research centres may be more likely to be sampled. Sites where high

Fig. 2 Spatial and temporal distributions of Data File 7. (a) The locations of mosquito collections of An. arabiensis, An. coluzzii and An. gambiae that were used to calculate $V_{gsc}$ allele frequencies. (b) The number of data points available for each year.
levels of resistance are expected may also be more likely to be sampled, as might sites where insecticide-based interventions are planned as a result of a combination of related variables. Geostatistical models can, however, be used to model sampling intensity to check these biases before proceeding further33.

Other data resources for insecticide resistance in malaria vector are available. Data on insecticide resistance in the *Anopheles* vectors of malaria are available from VectorBase, however, VectorBase's aim and scope are much broader than those of the current data release and the data volumes for insecticide resistance in *Anopheles* vectors are smaller than those provided here35. Furthermore, these data have not been configured specifically for use in mathematical analyses including geospatial analyses. Insecticide resistance data can also be viewed on interactive maps using the IR Mapper and Malaria Threats websites but these are data visualisation tools66. The data shown on these sites were not collated in support of mathematical analyses and are not available for download. There are overlaps in all of these databases, including overlaps with the data being released here. The data released here includes data that were provided to the World Health Organization to support the establishment of the Malaria Threats website66. In addition, the data being released here were shared with the group behind the IR Mapper site so that both groups could cross-check each other's sources to identify publications that had been missed.

A geo-database of insecticide resistance in the *Aedes* vectors of arboviruses has previously been released but this has much smaller data volumes for Africa, and encompasses a much greater range of insecticides tested at a greater range of concentrations on both adults and larvae35. In contrast, the data released here provide sufficient volumes of standardised values to support a range of analyses of insecticide resistance in malaria vectors in Africa and are freely available to all. In addition to the current data release, these data have been shared with the Pan Africa Mosquito Control Association to support the establishment of an Africa-led and -managed data resource. The datasets released here will also be available for download from the IR Mapper website [www.irmapper.com](http://www.irmapper.com).

In addition, predicted values for the prevalence of resistance (i.e. mortality in a standard WHO susceptibility test) at every location in a ~5 km resolution grid, for each year from 2005 to 2017, will be modelled and released in the coming months.

**References**

1. Hemingway, J. et al. Averting a malaria disaster: will insecticide denial derail malaria control? Lancet **387**, 1785–1788, [https://doi.org/10.1016/s0140-6736(15)00417-1](https://doi.org/10.1016/s0140-6736(15)00417-1) (2016).
2. Raoult, D. & Abat, C. Developing new insecticides to prevent chaos: the real future threat. Lancet Infectious Diseases **17**, 804–+, [https://doi.org/10.1016/s1473-3099(17)30395-7](https://doi.org/10.1016/s1473-3099(17)30395-7) (2017).
3. Cook, J. et al. Implications of insecticide resistance for malaria vector control with long-lasting insecticidal nets: trends in pyrethroid resistance during a WHO-coordinated multi-country prospective study. Parasites & Vectors **11**, [https://doi.org/10.1186/s13071-018-3101-4](https://doi.org/10.1186/s13071-018-3101-4) (2018).
4. Kleinschmidt, I. et al. Implications of insecticide resistance for malaria vector control with long-lasting insecticidal nets: a WHO-coordinated, prospective, international, observational cohort study. Lancet Infectious Diseases **18**, 640–649, [https://doi.org/10.1016/s1473-3099(18)30172-5](https://doi.org/10.1016/s1473-3099(18)30172-5) (2018).
5. Eisen, L. et al. Multi-Disease Data Management System Platform for Vector-Borne Diseases. Plos Neglected Tropical Diseases **5**, [https://doi.org/10.1371/journal.pntd.0001016](https://doi.org/10.1371/journal.pntd.0001016) (2011).
6. Kiware, S. S. et al. A generic schema and data collection forms applicable to diverse entomological studies of mosquitoes. Source Code for Biology and Medicine **11**, [https://doi.org/10.1186/s13029-016-0650-1](https://doi.org/10.1186/s13029-016-0650-1) (2016).
7. Massey, N. C. et al. A global bionomic database for the dominant vectors of human malaria. Scientific Data **3**, [https://doi.org/10.1038/sdata.2016.14](https://doi.org/10.1038/sdata.2016.14) (2016).
8. Mitsakakis, K. et al. Converging Human and Malaria Vector Diagnostics with Data Management towards an Integrated Holistic One Health Approach. International Journal of Environmental Research and Public Health **15**, [https://doi.org/10.3390/ijerph15020259](https://doi.org/10.3390/ijerph15020259) (2018).
9. Moyes, C. L., Temperley, W. H., Henry, A. J., Burgert, C. R. & Hay, S. I. Providing open access data online to advance malaria research and control. Malaria Journal **12**, [https://doi.org/10.1186/1475-278X-12-161](https://doi.org/10.1186/1475-278X-12-161) (2013).
10. Pfeffer, D. A. et al. MalariaAtlas: an R interface to global malariometric data hosted by the Malaria Atlas Project. Malaria Journal **17**, [https://doi.org/10.1186/s12936-018-2500-5](https://doi.org/10.1186/s12936-018-2500-5) (2018).
11. Browne, A. J. et al. The contemporary distribution of *Trypanosoma cruzi* infection in humans, alternative hosts and vectors (vol 4, 170050, 2017). *ScientificData* **4**, [https://doi.org/10.1038/sdata.2017.71](https://doi.org/10.1038/sdata.2017.71) (2017).
12. Ceccarelli, S. et al. DataTri, a database of American triatomine species occurrence. *Scientific Data* **5**, [https://doi.org/10.1038/sdata.2018.71](https://doi.org/10.1038/sdata.2018.71) (2018).
13. Coleman, M. et al. Developing global maps of insecticide resistance risk to improve vector control. *Malaria Journal* **16**, [https://doi.org/10.1186/s12936-017-1733-z](https://doi.org/10.1186/s12936-017-1733-z) (2017).
14. Killeen, G. F., Chaki, P. P., Reed, T. E., Moyes, C. L. & Govella, N. J. In *Towards Malaria Elimination* (eds Manguin, S. & Dev, V.), 403–429 (TeffchOpen, 2018).
15. Hancock, P. A. et al. Associated patterns of insecticide resistance in field populations of malaria vectors across Africa. *Proceedings of the National Academy of Sciences of the United States of America* **115**, 5938–5943, [https://doi.org/10.1073/pnas.1801826115](https://doi.org/10.1073/pnas.1801826115) (2018).
16. WHO Division of Malaria and Other Parasitic Diseases. Manual on practical entomology in malaria: part II methods and techniques. 197 (Geneva, 1975).
17. WHO Global Malaria Programme. Test procedures for insecticide resistance monitoring in malaria vector mosquitoes, 2nd edition. 55 (Geneva, 2016).
18. World Health Organization. Insecticide resistance and vector control: thirteenth report of the WHO Expert Committee on Insecticides. 106 (Geneva, 1963).
19. World Health Organization. Insecticide resistance and vector control: seventeenth report of the WHO Expert Committee on Insecticides. 94 (Geneva, 1970).
20. World Health Organization. Resistance of vectors and reservoirs of disease to pesticides: twenty second report of the WHO expert committee on insecticides. 88 (Geneva, 1976).
21. World Health Organization. Fifth report of the WHO Expert Committee on Vector Biology and Control: resistance of vectors of disease to pesticides. 82 (Geneva, 1980).
22. World Health Organization. Instructions for determining the susceptibility or resistance of adult mosquito to organochlorine, organophosphate and carbamate insecticides-diagnostic tests. (Geneva, 1981).
23. World Health Organization. Tenth report of the WHO Expert Committee on Vector Biology and Control: resistance of vectors and reservoirs of disease to pesticides. 88 (Geneva, 1986).
24. World Health Organization. Fifteenth report of the WHO Expert Committee on Vector Biology and Control: vector resistance to pesticides. 68 (Geneva, 1992).
25. World Health Organization. Test procedures for insecticide resistance monitoring in malaria vectors: bio-efficacy and persistence of insecticides on treated surfaces. 46 (World Health Organization, Geneva, 1998).
26. World Health Organization. Test procedures for insecticide resistance monitoring in malaria vector mosquitoes. 40 (Geneva, 2013).
27. Brogdon, W. & Chan, A. Guideline for evaluating insecticide resistance in vectors using the CDC bottle bioassay. 28 (Atlanta, 1998).
28. Moyes, C. L. et al. Data from: Analysis-ready datasets for insecticide resistance phenotype and genotype frequency in African malaria vectors. Dryad Digital Repository, https://doi.org/10.5061/dryad.dn4676s (2019).
29. Giorgi, E., Diggle, P. J., Snow, R. W. & Noor, A. M. Geostatistical Methods for Disease Mapping and Visualisation Using Data from Spatio-temporally Referenced Prevalence Surveys. International Statistical Review 86, 571–597, https://doi.org/10.1111/insr.12268 (2018).
30. Wiibe, A. et al. Geographical distributions of African malaria vector sibling species and evidence for insecticide resistance. Malaria Journal 16, https://doi.org/10.1186/s12936-017-1734-y (2017).
31. Moyes, C. L. et al. Predicting the geographical distributions of the macaque hosts and mosquito vectors of Plasmodium knowlesi in forested and non-forested areas. Parasites & Vectors 9, https://doi.org/10.1186/s12971-016-1527-0 (2016).
32. Gaughan, A. E., Stevens, F. R., Linard, C., Patel, N. N. & Tatem, A. J. Exploring nationally and regionally defined models for large area population mapping. International Journal of Digital Earth 8, 989–1006, https://doi.org/10.1080/17538947.2014.965761 (2015).
33. Golding, N. et al. Mapping under-5 and neonatal mortality in Africa, 2000-15: a baseline analysis for the Sustainable Development Goals. Lancet 390, 2171–2182, https://doi.org/10.1016/s0140-6736(17)31758-0 (2017).
34. Pafi, D., Reich, B. J. & Dunson, D. B. Bayesian geostatistical modeling with informative sampling locations. Biometrika 98, 35–48 (2010).
35. Lawson, D. et al. VectorBase: a data resource for invertebrate vector genomics. Nucleic Acids Research 37, D583–D587, https://doi.org/10.1093/nar/gkn857 (2009).
36. Knox, T. B. et al. An online tool for mapping insecticide resistance in major Anopheles vectors of human malaria parasites and review of resistance status for the Afrotropical region. Parasites & Vectors 7, https://doi.org/10.1186/1756-3305-7-76 (2014).
37. Mnzava, A. P. et al. Implementation of the global plan for insecticide resistance management in malaria vectors: progress, challenges and the way forward. Malaria Journal 14, https://doi.org/10.1186/s12936-015-0693-4 (2015).
38. Moyes, C. L. et al. Current status of insecticide resistance in the major Aedes vectors of arboviruses infecting humans. Plos Neglected Tropical Diseases 11, https://doi.org/10.1371/journal.pntd.0005625 (2017).

Acknowledgements
The preparation of this geospatial data resource was funded by the Wellcome Trust (grant 108440/Z/15/Z) and initial scoping work was funded by the Bill & Melinda Gates Foundation via the Vector-borne Disease Network (VecNet). The U.S. President's Malaria Initiative provided resistance data collected through PMI Africa Indoor Residual Project from several countries in Africa.

Author Contributions
C.L.M. devised the analysis-ready datasets for release. C.L.M. and A.W. drafted the data extraction and geopositioning protocols. A.W., K.G. and A.T. extracted, processed and geopositioned the data with guidance from C.L.M. and M.C. A.W. classified the species identification methods. K.G. extracted recommended sample sizes, doses and exposure durations from the WHO and CDC protocols. A.T. and A.W. identified duplicates in the data. C.L.M. checked the above work and reviewed the data. C.F., C.M., M.J.D., R.K.D., H.K., D.D., A.-N.C., E.O., S.A.A., A.S., C.S.M. and G.G.P. provided large volumes of unpublished data and provided advice on the use and format of these data. P.H., M.C. and C.L.M. contributed to the potential dataset uses.

Additional Information
Supplementary Information is available for this paper at https://doi.org/10.1038/s41597-019-0134-2.

Competing Interests: The authors declare no competing interests.

Publisher’s note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

The Creative Commons Public Domain Dedication waiver http://creativecommons.org/publicdomain/zero/1.0/ applies to the metadata files associated with this article.

© The Author(s) 2019