Course Map

Course Title
Short Course in Interpreting Malaria Molecular Surveillance Data
Course Goal
The goal of this course is to equip researchers, students, and public health officials with the knowledge and skills needed to effectively use malaria genomic data in epidemiological research and public health decision-making.
Course Learning Outcomes (CLOs)
By the end of the course learners will be able to: (1) Summarize the basic concepts and main use cases of malaria genomic epidemiology. (2) Choose the appropriate metrics derived from malaria genomic data to answer key questions. (3) Choose the appropriate molecular methods used to generate genomic data for different use cases and settings. (4) Design malaria molecular surveillance studies to answer key questions about the epidemiology of malaria. (5) Interpret results derived from molecular data to make sound public health recommendations.
Course Format
This course is fully online. Content is delivered asynchronously, meaning learners can complete the course independently their own pace. We estimate that most learners will complete the course in 10-12 total hours. The course content includes a mix of short video lectures, interactive case studies, knowledge checks, job aids, and moderated discussion forums.

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M0-Malaria 101-A Prelude to Genetic Surveillance Lead: Will Secondary: Bryan	(0) review foundational knowledge to facilitate learning in remainder of the course *Note: this is intended to be a review for most learners*.	(0.1) Identify the species of parasites causing malaria, describe their geographic distribution, lifecycle, and consequences of infection from severe disease through asymptomatic infection. (0.2) Identify the major species of mosquitos transmitting malaria, describe key aspects of human-mosquito interactions e.g. where and when biting occurs, and methods for quantifying mosquito abundance, vector composition, timing and location of biting, etc. (0.3) Identify means for diagnosis and case management of malaria (microscopy, RDT, ACTs), along with key interventions including vector control (LLIN, IRS, spatial repellents, …), chemoprevention (IPTi, IPTp, SMC, PMC, …), immunologic (vaccines, monoclonal antibodies). (0.4) Identify key partners in controlling malaria, e.g. NMCPs, WHO, research	**Watch Lecture Videos:** LV0-Background of Malaria Genetic Epidemiology AS0- multiple-choice quiz	**Complete quiz:** AS0- multiple-choice quiz

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		groups, Africa CDC, Global Fund, …		
M1– Malaria Epidemiology and Surveillance Lead: Amy Secondary: Bryan	(1) Summarize the basic concepts and main use cases of malaria genomic epidemiology.	By the end of this module learners will be able to: (1.1) Describe the main methods used in traditional surveillance, what information they can provide, and limitations. (1.2) Describe the main use-cases of malaria molecular surveillance. (1.3) Recognize the things you can and can't do with traditional vs. genetic surveillance (1.4) Calculate and interpret common measurements of traditional surveillance (incidence, prevalence, HBR, SIR, VA, EIR).	**Lecture Videos and Activities** LV1.1-overview-of-malaria-surveillance-and-epidemiology LV1.2-common-malaria-surveillance-metrics AC1.1-recognize-common-malaria-metrics-and-use-cases LV1.3-what-traditional-malaria-surveillance-can-miss AC1.2-explore-how-studies-and-measurements-can-help inform-malaria-surveillance. **Job Aids:** JA1.1-Malaria-Genomic-Epi-Glossary JA1.2-Malaria-Genomic-Epi-Use-Cases-QuickReference *Includes comparison of traditional vs molecular methods*	AS1- Multiple choice quiz on the basic concepts and use-cases of malaria genomic epidemiology AND Short answer questions that require learners to explain the use-cases and basic concepts of malaria genomic epidemiology. ***Note**: Assessments will integrate variations of knowledge checks and cases studies listed in the "Activities and Materials" column for this module.*
M2-Basics of Malaria Genetic Surveillance Lead: Bryan Secondary: Amy	(1) Summarize the basic concepts and main use cases of malaria genomic epidemiology.	(2.1) Identify relationships between transmission and the fundamental aspects of genetics based on basic transmission biology.	**Watch Lectures Videos:** LV2.1-genetic-variation-v9-6-23.pptx LV2.2-malaria-transmission-polyclonal infections-and-sexual-recombination-v9-12-23.pptx	AS2 Multiple choice quiz on the basic concepts and use-cases of malaria genomic epidemiology

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		(2.2) Discuss key terms for genetic variation, how this variation is generated in malaria and the mosquito vector, and how this differs from other pathogens and humans. (2.3) Correctly interpret simple phenotypes (resistant / not resistant) from malaria parasite and vector genotype data ~~(2.4) Identify the current landscape of molecular data in guiding decisions, including organizations which are integrating these data into surveillance (Africa CDC, public health and research organizations) and real-world examples of where these data are guiding decisions, e.g. Mekong region and ART-R, SMC or MDA in Gambia, HRP2 deletion and changing RDTs~~.	LV2.3-measuring-genetic-variation-snps-v9-6-23.pptx LV2.4-measuring-genetic-variation-haplotypes.pptx LV2.5-other-types-of-variation-and-brief-overview-on-methods-to-measure-them .pptx LV2.6-current-landscape-of-molecular-data-in-guiding-decisions.pptx **Review Job Aids** JA2.1-Malaria Genomic Epi Use Cases Quick Reference (including comparison of traditional vs molecular methods) JA2.3-Estimating MOI using different approaches. **Complete Interactive Activities** AC2.1 – Knowledge check questions on genotype and phenotype AC2.2 - Interpret simple genotypes (e.g. 3 SNP loci) in terms of mono/polyclonal, which haplotypes may be present. AC2.2 – Malaria transmission and genetic diversity AC2.3 – Knowledge check questions on measuring SNPs AC2.4 – Genotype sleuthing: SNPs and MOI AC2.5 – Interpreting SNPs and haplotypes in polyclonal infections AC2.6 – Genotype sleuthing: SNPs, microhaplotypes, and MOI (oh my!)	AND Short answer questions that require learners to explain the use-cases and basic concepts of malaria genomic epidemiology. ***Note**: Assessments will integrate variations of knowledge checks and cases studies listed in the "Activities and Materials" column for this module.*

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			AC2.7 – Knowledge check questions-basic concepts of types of mutations and ways to measure them	
M3 – Drug and Diagnostic Resistance Andres	(1) Summarize the basic concepts and main use cases of malaria genomic epidemiology.	3.1. Explain the link between changes in DNA and resistance phenotypes in the parasite and the vector. Especially, explain the link between genotypes in an infection and the expected outcome of treatment 3.2. Discuss the complexity of the link between genotype, phenotype, treatment outcomes and decision making 3.3. Explain how phenotypes conferring selective advantage can result in selection and spread of mutations 3.4. Enumerate traditional studies to evaluate drug and	JA1.3.1 Genetic variation review (review SNP, microsatellite, microhaplotypes) LV3.0 - Introduction to resistance LV3.1 - Drug and insecticide resistance LV3.2 - Field studies for drug resistance introduction LV3.3 - Molecular mechanisms of resistance AC3.1 Smarties activity (drug resistance) LV3.4 - Insecticide resistance LV3.5 - Selection and spread of resistance LV3.6 - TES LV3.7 - Diagnostics and species identification LV3.8 - Biological basis of diagnostic resistance + field studies	

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		insecticide resistance, and argue why you would perform a TES, in vitro study of parasite resistance and/or monitor molecular markers to perform surveillance for drug resistance 3.5. Explain how parasites are identified and how DNA can be used as an identifier and to measure parasitemia 3.6 Compare different diagnostic methods 3.7 Describe strategies to track diagnostic failures in the field 3.8 Interpret results from drug resistance studies (mms, in-vivo lab, and TES)		
M4-Genetic Data Generation,	(2) Choose the appropriate molecular	(4.1) Recognize the strengths & weaknesses of different	LV4.1 – Basic genotyping methods	AS4- Case studies that ask learners to select the appropriate

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Interpretation, and Applications Lead: Andres Secondary: Bryan	methods to generate genomic data for different use cases (vector and parasite).	genotyping technologies (including sequencing) (4.2) Match appropriate technologies to different use-cases, (4.3) Identify economies of scale that inform choices on methods when wanting results to inform more than 1 question (4.4) Identify technical features of data that could bias affect results, or at least be aware that technical things COULD influence results, e.g. low density infections might have false negative alleles and underestimate MOI compared to higher density infections (4.5) Identify appropriate methods for identification of vector species and insecticide resistance.	LV4.2 – SNP genotyping pros and cons AC4.1 – knowledge check: choosing genotyping for SNPs LV4.3 – NGS motivated with microhaplotypes LV4.4 – Genotyping comparisons and use cases LV4.5 – Use cases for diagnostic resistance AC4.2 – matching activity: genotyping for parasites LV4.6 – Genotyping for vector species and insecticide resistance AC4.3 – genotyping for vectors LV4.7 – Bioinformatics AC4.4 – paper bioinformatics ~~**For researchers only:**~~ ~~LV4.1.R: Electrophoresis and capillary electrophoresis~~ ~~LV4.2.R: qPCR for parasitemia~~ ~~AC4.2.R: Interpret qPCR amplification curve and standard curve~~ ~~LV4.3.R: qPCR for SNPs~~	molecular method for a specific use-case and explain why they chose that method. AND Online simulation where learners have to choose the most cost-effective and efficient molecular method for generating genomic data for a particular use-case. ***Note** – can integrate into "study design" CLO, structure as a game where learners have fixed budget and had to try to answer a certain question. More simply, they could have a cost per sample and try to answer a set of questions with a fixed budget – smaller sample size with more expensive assays, but also some economy of scale with some

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			~~LV4.4.R: qPCR for CNV~~ ~~LV4.5.R: qPCR for deletions~~ ~~AC4.3.R: Interpreting results~~ - ~~(understand) classify examples into qualitative or quantitative rtPCR~~ - ~~(understand) identify mdr1 duplication in quantitative rtPCR results~~ - ~~(understand) identify hrp2 deletion in qualitative rtPCR results~~ - ~~(understand) identify crt mutation in qualitative rtPCR results~~ - ~~(apply) use results from qualitative rtPCR to infer genotypes in polyclonal infection~~ - ~~(evaluate) criticize use of quantitative rtPCR to infer deletions or duplications in polyclonal infections based on results~~ ~~LV4.6.R RFLP~~ ~~LV4.7.R: Sanger sequencing~~ ~~AC4.5.R: (apply) identify polyclonal infection in dhfr or dhps chromatogram results and explain limitation of that data to genotype such infection~~ ~~AC4.6.R: genotype infection using provided k13 sequencing result and reference sequence using blast~~ ~~AC4.7.R Activity: (apply) Choose the type of genetic variation to be genotyped in a given use case(s), and appropriate genotyping method~~	assays if multiple questions… ***Note**: Assessments will integrate variations of knowledge checks and cases studies listed in the "Activities and Materials" column for this module*

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			~~Other activities~~	
M5 – Using Genetic Diversity and Relatedness to Evaluate Transmission Lead: Bryan Secondary: Amy	(3) Choose the appropriate metrics derived from malaria genomic data to answer key questions.	(5.1) Recognize how measures of genetic diversity relate to transmission and can be derived from genetic data (5.2) Match measures of genetic diversity/differention to different epidemiological scenarios (5.3) recognize how measures of genetic relatedness relate to transmission and can be derived from genetic data (5.4) RESEARCH ONLY: Calculate IBS between sequences. Polyclonal measures, e.g. Jaccard index? (5.5) RESEARCH ONLY: Articulate the weaknesses of IBS and benefits of IBD. For example, above calculation for very low diversity locus -> high IBS but means very little. (5.6) Interpret genetic relationships between infections in terms of overall	LV5.1 – Intro to genetic measures of malaria transmission LV5.2 – Malaria transmission and within-host diversity (MOI) AC5.1 - Understanding MOI LV5.3 – Malaria transmission and population diversity (heterozygosity) AC5.2 – Malaria transmission and genetic diversity LV5.4 – Context for measures of transmission AC5.3 – Real data example of transmission and genetic diversity (two levels) ~~LV5.5 – Malaria transmission and within-host diversity 2 (beyond MOI) – **RESEARCH ONLY**~~ LV5.6 – Connectivity 1: Relatedness between populations (interpret Fst and Jost's D) AC5.4 – Assessing population measures of parasite connectivity AC5.4R – Assessing population measures of parasite connectivity (calculate Fst and Jost's D) – **RESEARCH ONLY** LV5.7 - Connectivity 2: Relatedness between infections A5.5 – Relatedness between infections check your knowledge. LV5.6 – Estimating relatedness from genetic data (IBS and IBD) - **RESEARCH ONLY**	

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		transmission intensity, case classification (5.7) OPTIONAL: Interpret genetic relationships between mosquitoes (population structure, gene flow) in terms of mosquito movement and spread of insecticide resistance. (5.8) Understand the limitation of data and how interpretation might vary in the context of important caveats. For example, can you confidently say that a case is imported vs. local? How might high rates of importation, and where they are imported from, affect other metrics such as MOI?	AC5.7 – Genotype sleuthing – estimating transmission networks from genetic data ~~LV5.8 – Transmission networks~~ JA5.1 Review of metrics and relationships with transmission intensity	
M6– Study Design for Malaria Molecular Surveillance Lead: Bob Secondary: Amy	(4) Design malaria molecular surveillance studies to answer key questions about the epidemiology of malaria.	(6.1) Describe how genomic surveillance can complement traditional surveillance. For example, the distinction between a therapeutic efficacy study and molecular surveillance for drug resistance. (6.2) Select the broad features of a survey (e.g. target population, geographic	LV6.1 – What motivates your study? LV6.2 – Factoring in the epidemiological setting LV6.3 – Defining the target population LV6.4 – Sampling from a population LV6.5 – Frequency of sampling LV6.8 – The key concept of statistical power LV6.9 – Power curves and sample size tables LV6.10 – Controlling the margin of error LV6.11 – Multi-cluster studies and the design effect LV6.12– The consequences of lower power	AS6.1- Multiple-choice questions interpreting differences between case-based questions, e.g. Mary wants to do spend the budget doing study A, Frank wants to do study B - which will be better at X? Why? Which will be better at Y? Why?

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		scale, stratification) for major use cases. (6.3) List the strengths and weaknesses of different sampling approaches, e.g., cluster sampling, cross sectional, cohort. (6.4) Define statistical terms, i.e. power, margin of error, minimum sample size. Interpret power curves and sample size tables. (6.5) Choose appropriate parameters for a multi-cluster power calculation. (6.6) List the negative effects of an underpowered study. (6.7) Critically evaluate different study designs with the aim of measuring connectivity / importation (6.8) Perform sample size & power calculation for these use-cases	AC6.1 - Match overall study design to research question. AC6.2– Match sampling approach to research question. **Review Job Aids:** JA6.1 - Study design, sampling tables, and statistical reference for malaria genomic surveillance. ~~JA6.3- Statistical Terms Quick Reference~~ ~~JA6.4-Sample size tables for common study designs~~ **Complete Interactive Activities** AC6.3 – Match terms against their definitions. AC6.4 – Interpret a power curve and sample size table AC6.5– Interpret a margin of error curve and sample size table ~~AC6.6– Design a pfhrp2/3 deletion study~~ **Watch Lecture Videos** LV6.13– Connectivity and Importation **Review Job Aids:** **NA** **Complete Interactive Activities**	What if the situation was changed such that …. AS6.2 - Case study with short answer questions that require learners to design a malaria molecular surveillance study to answer a specific research question AS4.3 – Case study with multiple choice questions where leaners will perform sample size & power calculation for use-cases for measuring connectivity and importation.

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		(6.9) Choose appropriate types of information to inform decisions about interventions. ***Note**: - TBD topic, may be beyond scope*	AC6.7 - Calculate sample size to have a good chance of seeing at least 10 IBD links given certain parameters AC6.8 - "Choose your own adventure" study designs following in the style of Jon Russel activity (fixed resources, choice of sites, data) but across a wider range of use cases and to demonstrate different specific points of interest. Allow users to follow a few different paths for each case and see the pros and cons of their choices. Can incorporate that "slider" idea above, perhaps after introduced on its own. Include examples focused on connectivity and transmission setting to highlight limitations of current approaches	
M7. Interpreting Results and Making Policy Recommendations Lead: Andres Secondary: All	(5) Interpret results derived from molecular data to make sound public health recommendations for malaria control.	(7.1) Correctly interpret combinations of results (e.g. traditional + MMS) in different scenarios (7.2) Choose between different ways of presenting results, based on the results and your audience (7.3) Identify misleading ways of presenting results. (7.4) Make sensible public health recommendations on the basis of MMS results	Watch Lectures LV7.1 -Case Studies in Malaria Genomic Epidemiology **Review Job Aids**: J7.1 - Interpreting Results Quick Reference ***Note** -for some typically expected results, what some reasonable next steps are. E.g. drug resistance mutation prevalence is nearly zero, continue intermittent surveillance. Slightly higher, consider intensifying surveillance. Moderate, start implementing therapeutic efficacy studies if not yet done. High, consider changing drug.* **Complete Interactive Activities** AC7.1 – Focus on interpreting these results and identifying next steps - Case studies combining concepts from earlier modules.	AS7.1 - Case studies that ask learners to interpret the results of molecular data in the context of standard epidemiological studies and make public health recommendations based on those results. AS7.2 - Online discussion forum where learners have to analyze and

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		(7.5) Choose between methods of presenting results to e.g. control program, scientists, laypeople.	Multi-step activity, i.e. select main interpretations from options and then make one final recommendation at the end – or in some situations there may be multiple valid next steps given a set of results. Learner can choose which steps are reasonable, and then answer questions regarding pros and cons of each. AC7.2 - Given different presentations of the same data, select the one that is clearest. AC7.3 - Choose presentation of data for a particular audience	interpret results from molecular data and discuss their implications for public health ***Note**: Assessments will integrate variations of knowledge checks and cases studies listed in the "Activities and Materials" column across ALL modules. .*