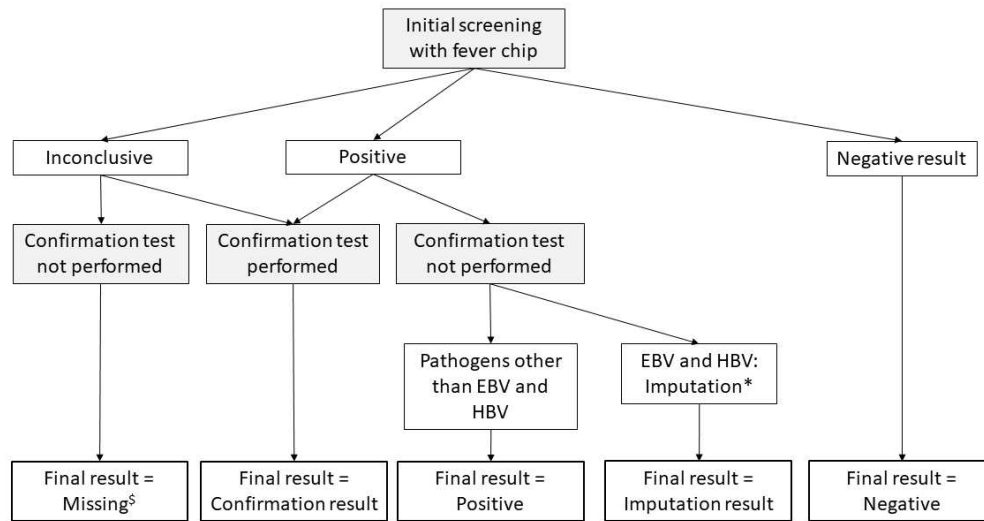


Supplemental Figures

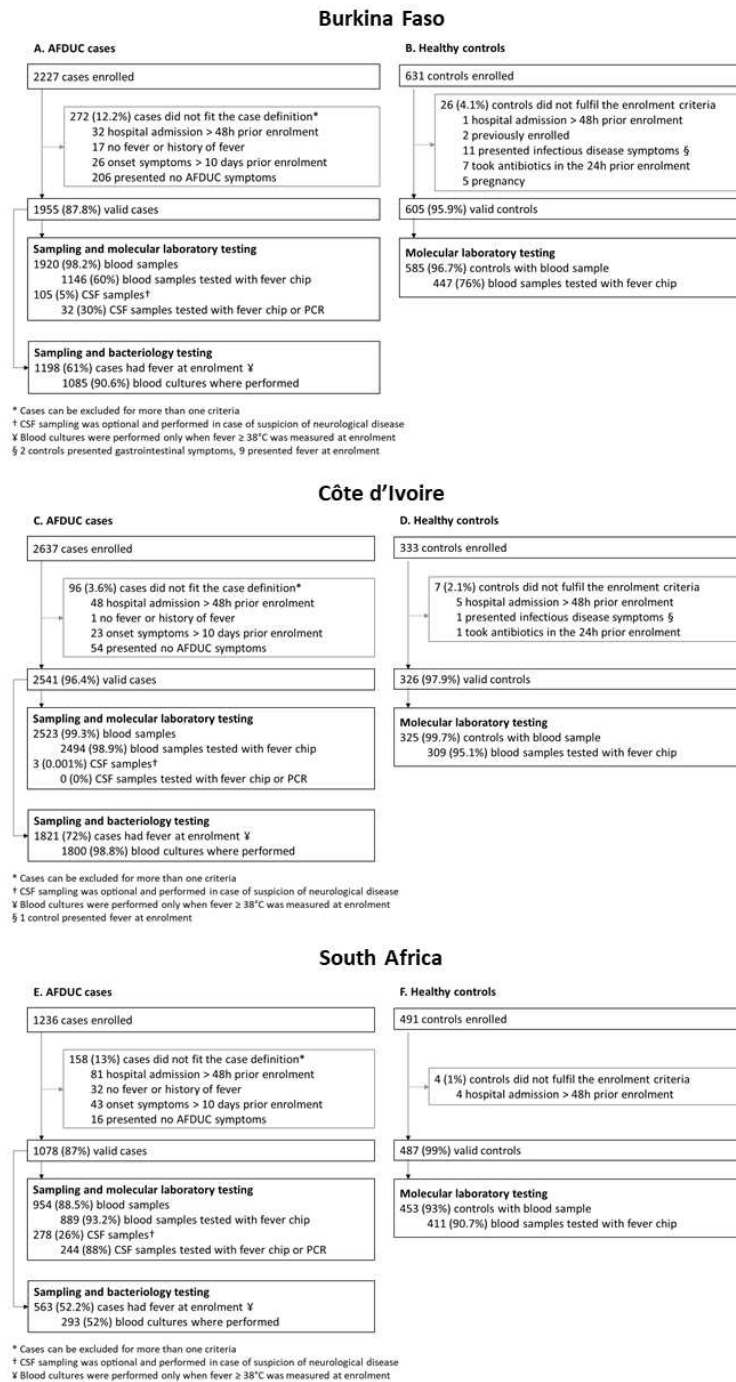
Supplemental Figure 1. Final result definition flowchart.	2
Supplemental Figure 2. AFDUC cases and healthy controls enrolment, sampling and testing per country.....	3
Supplemental Figure 3. HIV status distribution (%) in AFDUC cases and controls by age group and country.....	4
Supplemental Figure 4. HBV vaccination status distribution (%) in AFDUC cases and controls by age group and country.....	5
Supplemental Figure 5. Neurological symptom frequencies (%) in AFDUC cases which required hospitalisation by country and age group.....	6
Supplemental Figure 6. Neurological symptom frequencies (%) in AFDUC cases by country and hospitalisation status.....	7
Supplemental Figure 7. Overview of all blood test results by AFDUC/Control status and country.	8
Supplemental Figure 8. Detection rates, based on fever chip, confirmation PCR and imputation, of major pathogens across countries and specimen types.....	9
Supplemental Figure 9. Detection rates (%) in blood in AFDUC cases and controls stratified by country and residence or age group.	10
Supplemental Figure 10. Detection rates (%) of EBV, HBV and <i>P. falciparum</i> in blood samples from AFDUC cases and controls by country and month of enrolment.	11
Supplemental Figure 11. Detection rates (%) of EV and AdV in blood samples from AFDUC cases and controls in SA by month of enrolment.	12
Supplemental Figure 12. Detection rates (%) of DENV and CHIKV IgM in cases in BF and CI.	13
Supplemental Figure 13. Detection rates in blood culture and bacterial species identified.	14



*Imputation was only performed for EBV and HBV as they had a proportion of positives greater than 1% and sufficient confirmation PCR test results
[§]Missing results were excluded from the final analysis

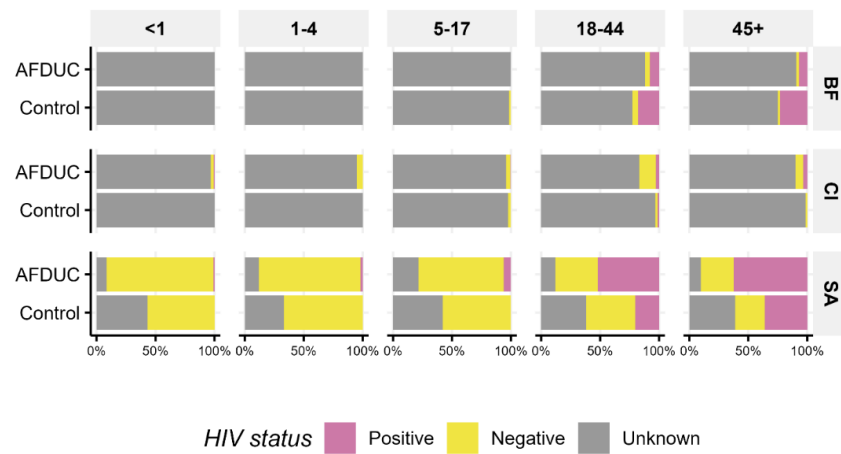
Supplemental Figure 1. Final result definition flowchart.

The final result is based on results obtained from fever chip, confirmation PCR and multiple imputation for EBV and HBV. Multiple imputation was applied to replace missing confirmation PCR results among cases/controls with positive fever chip results.

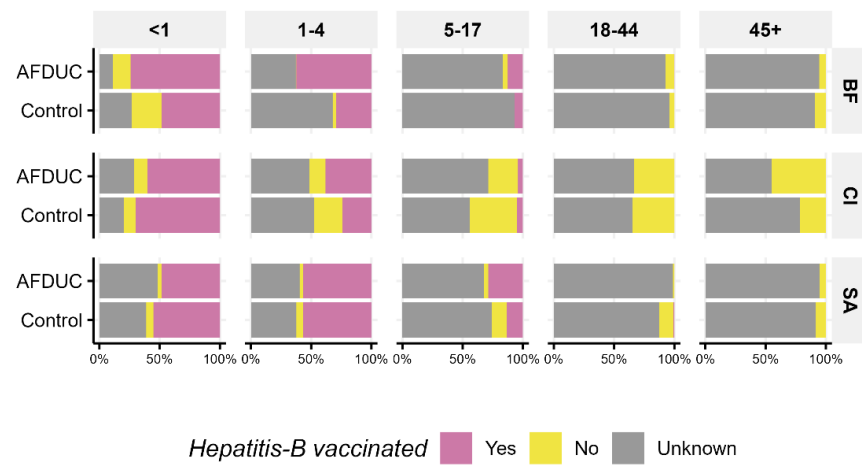


Supplemental Figure 2. AFDUC cases and healthy controls enrolment, sampling and testing per country.

(A) Number of cases and (B) controls in BF. (C) Number of cases and (D) controls in CI. (E) Number of cases and (F) controls in SA. CSF: Cerebrospinal fluid; blood samples refers to EDTA blood specimens and sera.

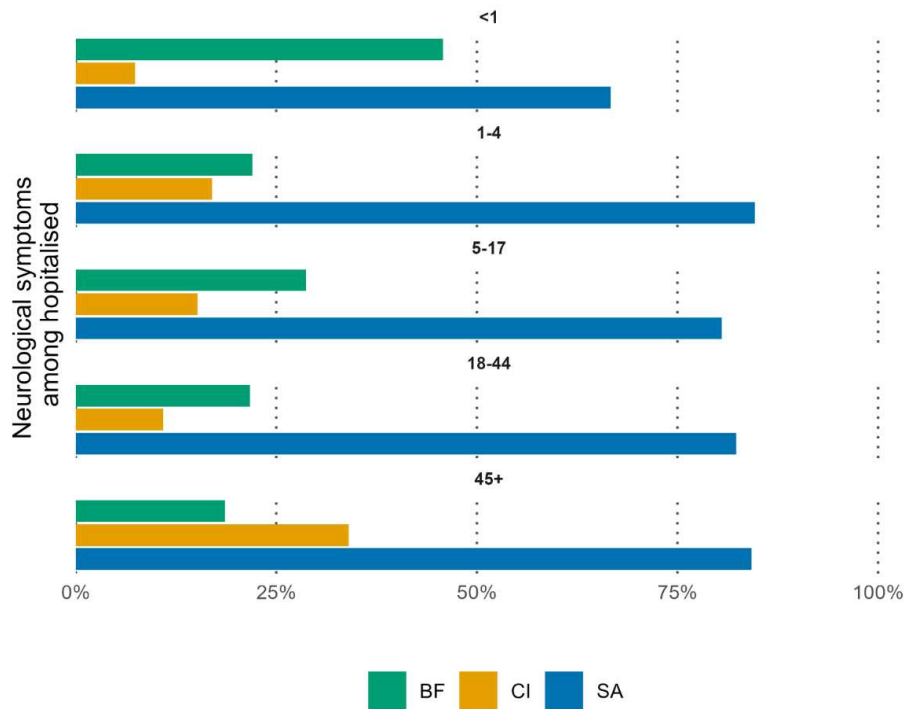


Supplemental Figure 3. HIV status distribution (%) in AFDUC cases and controls by age group and country. Proportions of HIV status in each age group are shown. Cases and controls with missing age are excluded (n = 6).



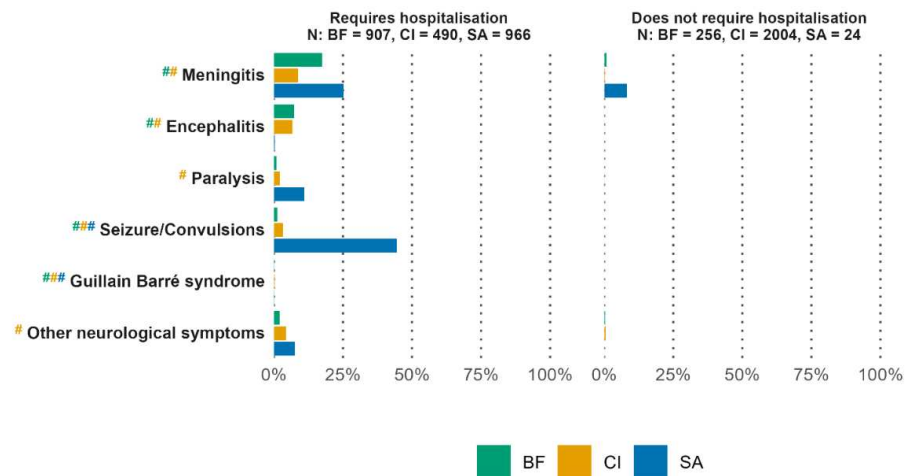
Supplemental Figure 4. HBV vaccination status distribution (%) in AFDUC cases and controls by age group and country.

Proportions of Hepatitis-B vaccination status in each age group are shown among all cases and controls. Cases and controls with missing age are excluded (n = 6).



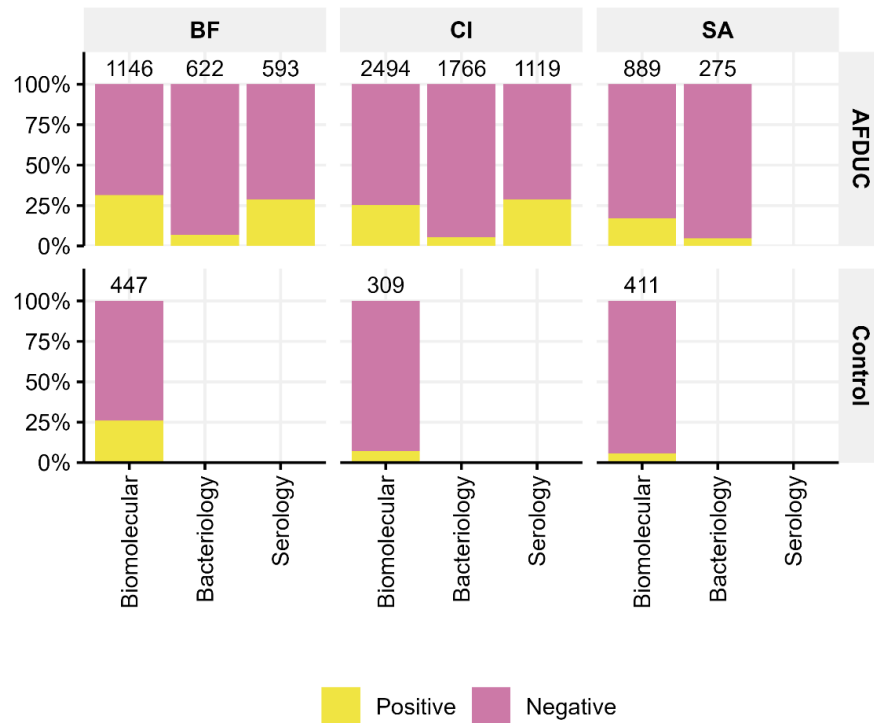
Supplemental Figure 5. Neurological symptom frequencies (%) in AFDUC cases which required hospitalisation by country and age group.

Frequencies represent the ratio of cases requiring hospitalisation with neurological symptoms by the total number of cases requiring hospitalisation by age group and country. Two cases were excluded in SA due to missing age. The denominators are given by (BF, CI, SA): <1 (72, 27,201), 1-4 (236,141,435), 5-17 (160,66,113), 18-44 (240, 156, 158), 45+ (199,100,57).



Supplemental Figure 6. Neurological symptom frequencies (%) in AFDUC cases by country and hospitalisation status.

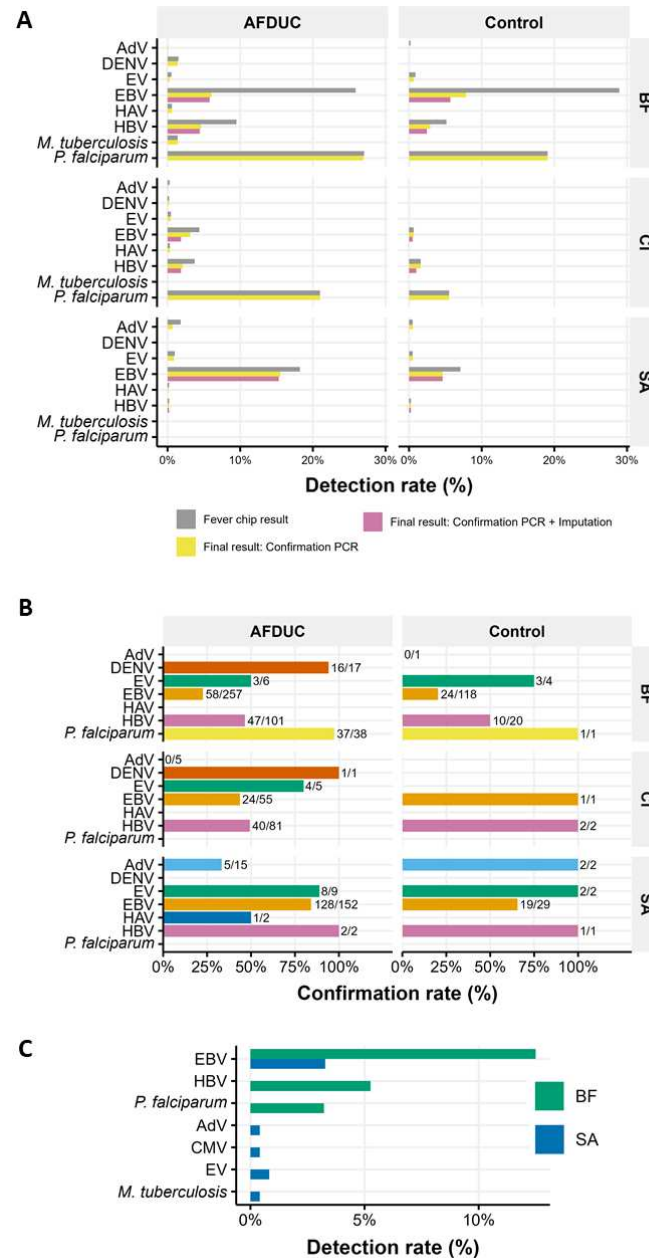
Neurological symptoms are shown and frequencies are computed among all cases including those without neurological symptoms. The left panel shows percentages among cases requiring hospitalisation. The right panel shows percentages among cases not requiring hospitalisation. One case in BF and one case in SA are excluded due to missing hospitalisation data. Hashtags next to the symptoms' names indicate significant difference ($p < 0.05$) for chi-squared (or Fisher exact) test for differences in the frequency of reported symptoms by hospitalisation status. The colour of the hashtag corresponds to the country for which this difference was significant.



Supplemental Figure 7. Overview of all blood test results by AFDUC/Control status and country.

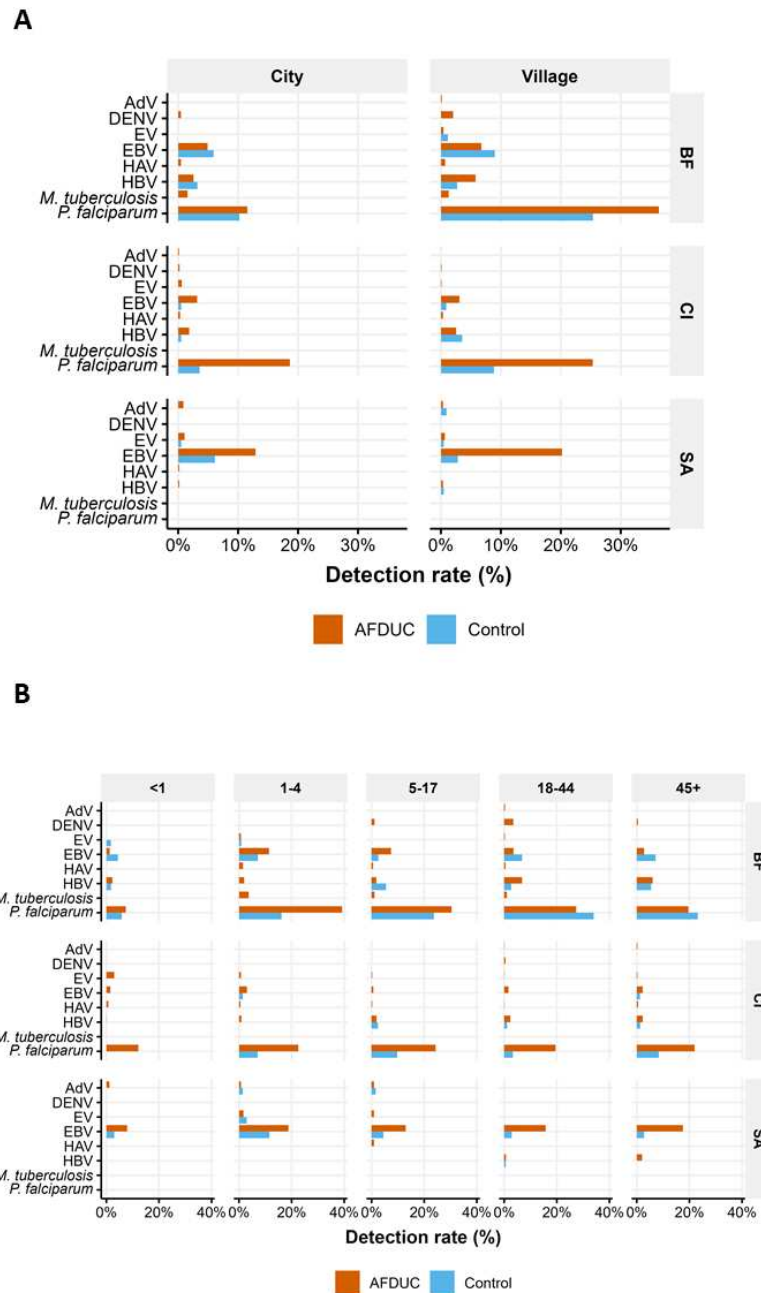
Detection rates (yellow) for any pathogen identified by biomolecular, bacteriological and serological tests are shown.

Denominators above the bars indicate the number of samples tested by the respective method. For each method, detection rates correspond to the proportion of cases or controls with a positive result for any virus, bacteria or parasite among all individuals tested using that method. Biomolecular results are based on the final result variable. Bacteriological results are restricted to cases presenting with measured fever at enrolment. Serological analysis combines DENV and CHIKV results and includes only cases from BF and CI and was conducted primarily on adult cases.



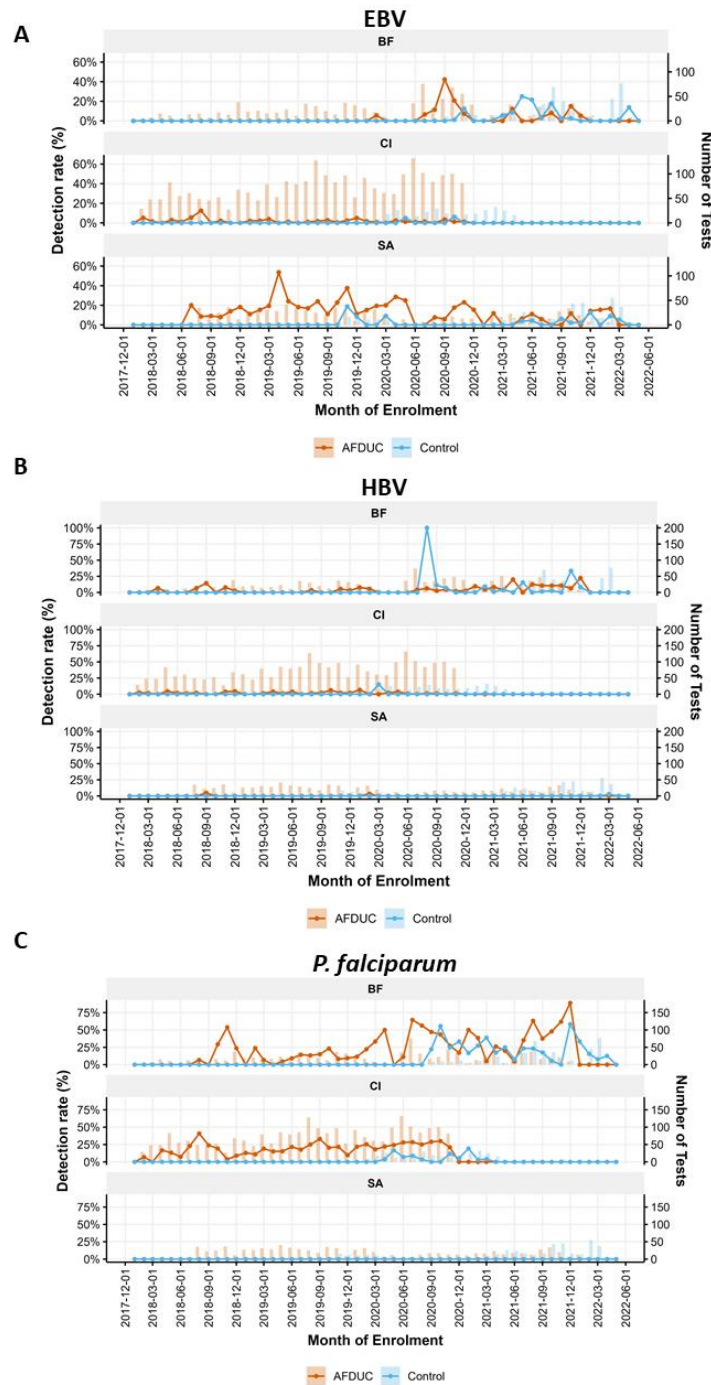
Supplemental Figure 8. Detection rates, based on fever chip, confirmation PCR and imputation, of major pathogens across countries and specimen types.

A. Comparison of detection rates (%) in blood samples from the fever chip, confirmation PCR, and imputed results (EBV & HBV only), stratified by case/control status and country. B. Confirmation rates (%) in blood samples for each pathogen, calculated as the proportion of PCR-confirmed fever chip positives, stratified by case/control status and country. Only pathogens with ≥ 10 detections are shown. C. Detection rates (%) in CSF samples from AFDUC cases in BF and SA based on combined fever chip and confirmation PCR results. Denominators: SA (N = 244); BF—EBV (N = 32), HBV (N = 19), *P. falciparum* (N = 31). Note: “Final result: Confirmation PCR + Imputation” applies only to EBV and HBV (see Supplemental Figure 1). Fever chip detection rates exclude inconclusive results from denominators.



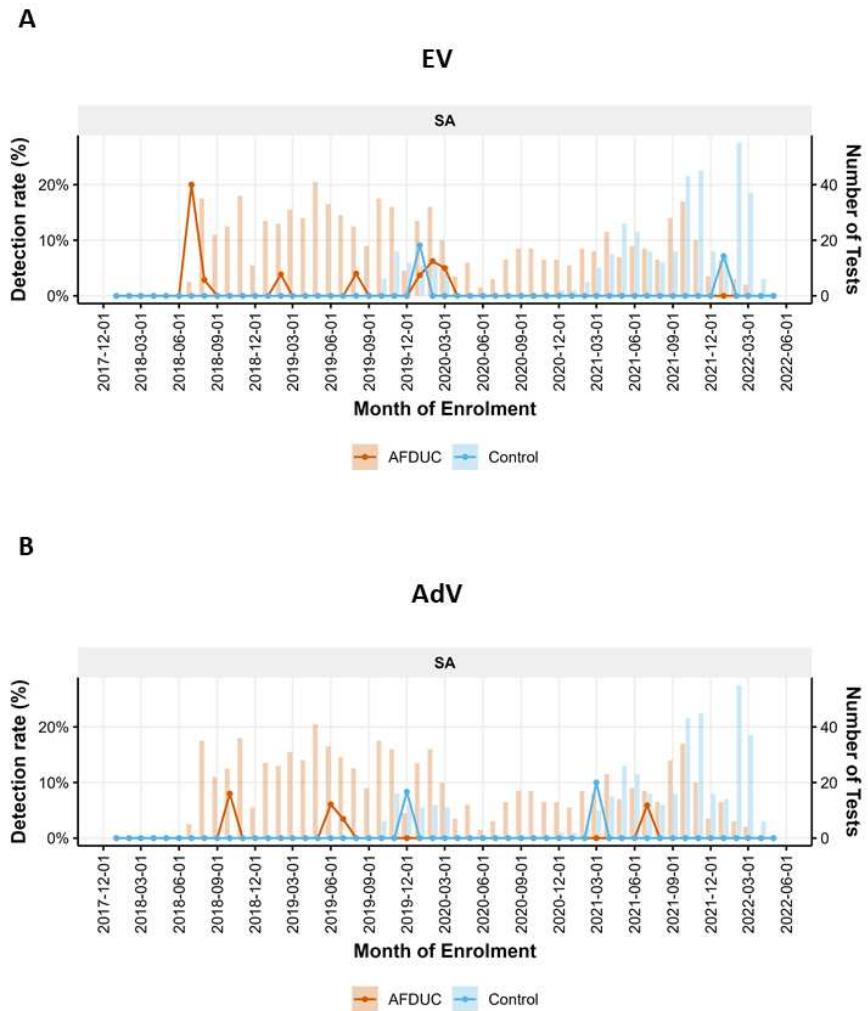
Supplemental Figure 9. Detection rates (%) in blood in AFDUC cases and controls stratified by country and residence or age group.

A. Detection rates by country and residence were correspond to the ratio of number of positives over number of tested using the final result. Cases and controls with missing residence are excluded ($n = 22$). B. Detection rates by country and age group correspond to the ratio of number of positives over number of tested using the final result. Cases and controls with missing age were excluded ($n = 5$). Note: Only pathogens with at least ten detections on the fever chip for cases or controls are shown.



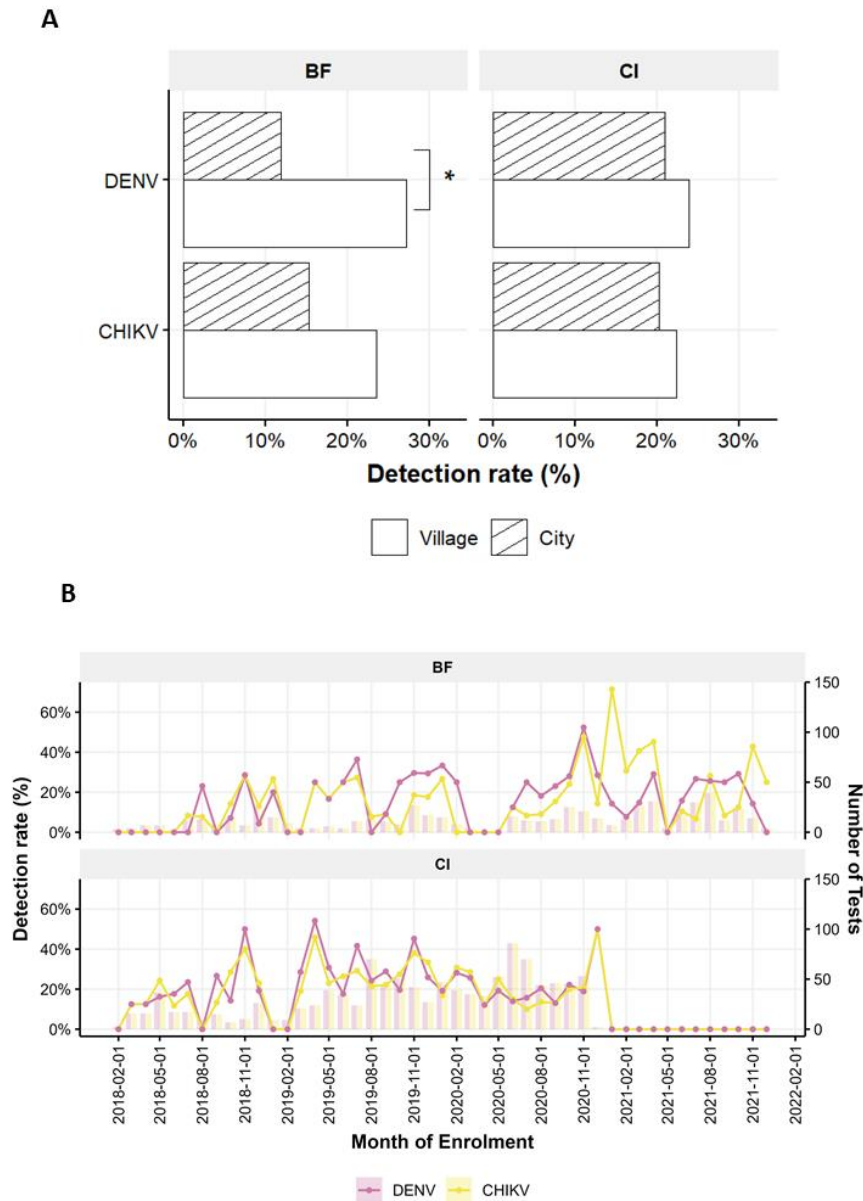
Supplemental Figure 10. Detection rates (%) of EBV, HBV and *P. falciparum* in blood samples from AFDUC cases and controls by country and month of enrolment.

A. EBV, B. HBV, C. *P. falciparum*. detection rates are shown as lines with the number of tests performed shown as bars in the background. Detection rates were computed using the final result and taking the ratio of number of positives over number of tested.



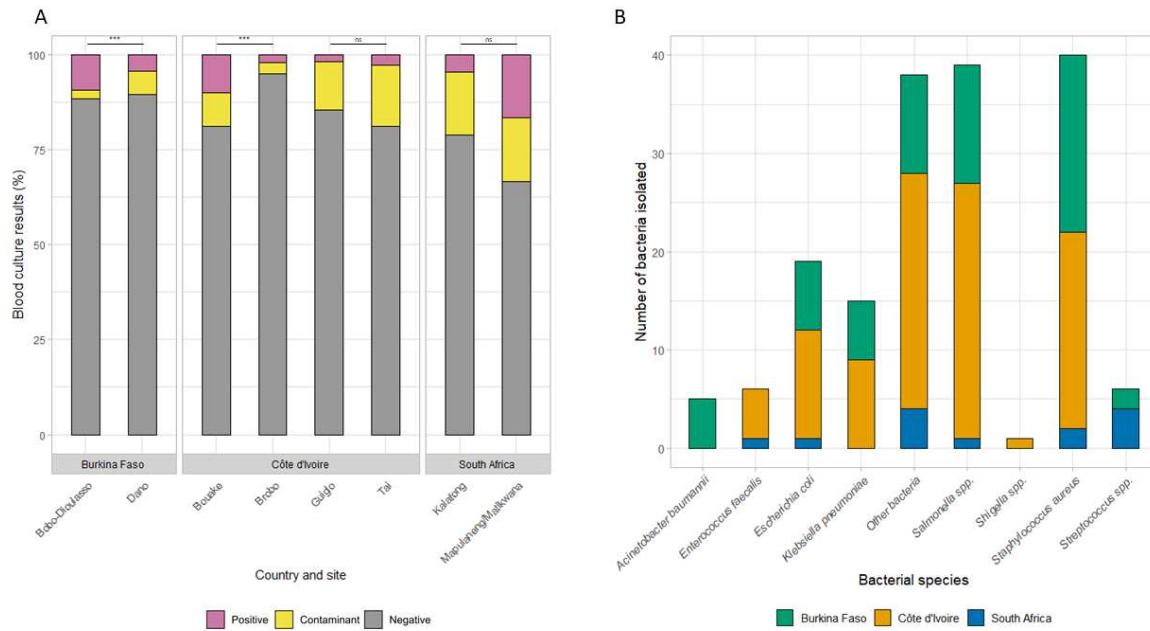
Supplemental Figure 11. Detection rates (%) of EV and AdV in blood samples from AFDUC cases and controls in SA by month of enrolment.

A. EBV, B. AdV. Detection rates are shown as lines with the number of tests performed shown as bars in the background. Detection rates were computed using the final result and taking the ratio of number of positives over number of tested.



Supplemental Figure 12. Detection rates (%) of DENV and CHIKV IgM in cases in BF and CI.

A. Detection rates by country and residence are shown as bars and significant differences (p -value < 0.05) in detection rates by residence tested by multivariable logistic regression are indicated with *. The adjustment set consists of age group, sex, month of enrolment, year of enrolment and HIV status. Two cases with serological results from BF are excluded due to missing residence information. B. Detection rates by country and month of enrolment are shown as line with the number of tests performed shown as bars in the background. Detection rates were computed using the ELISA test result from serology and taking the ratio of number of positives over number of tested.



Supplemental Figure 13. Detection rates in blood culture and bacterial species identified.

A. Blood cultures detection rates per site and country, BF (N=622), CI (N=1766) and SA (N=275); significant differences (p-value < 0.0001) obtained by Chi-squared or Fischer tests are indicated with ***, non-significant results are indicated with ns.

B. Bacterial species identified in blood cultures per country.