

Supplementary figures

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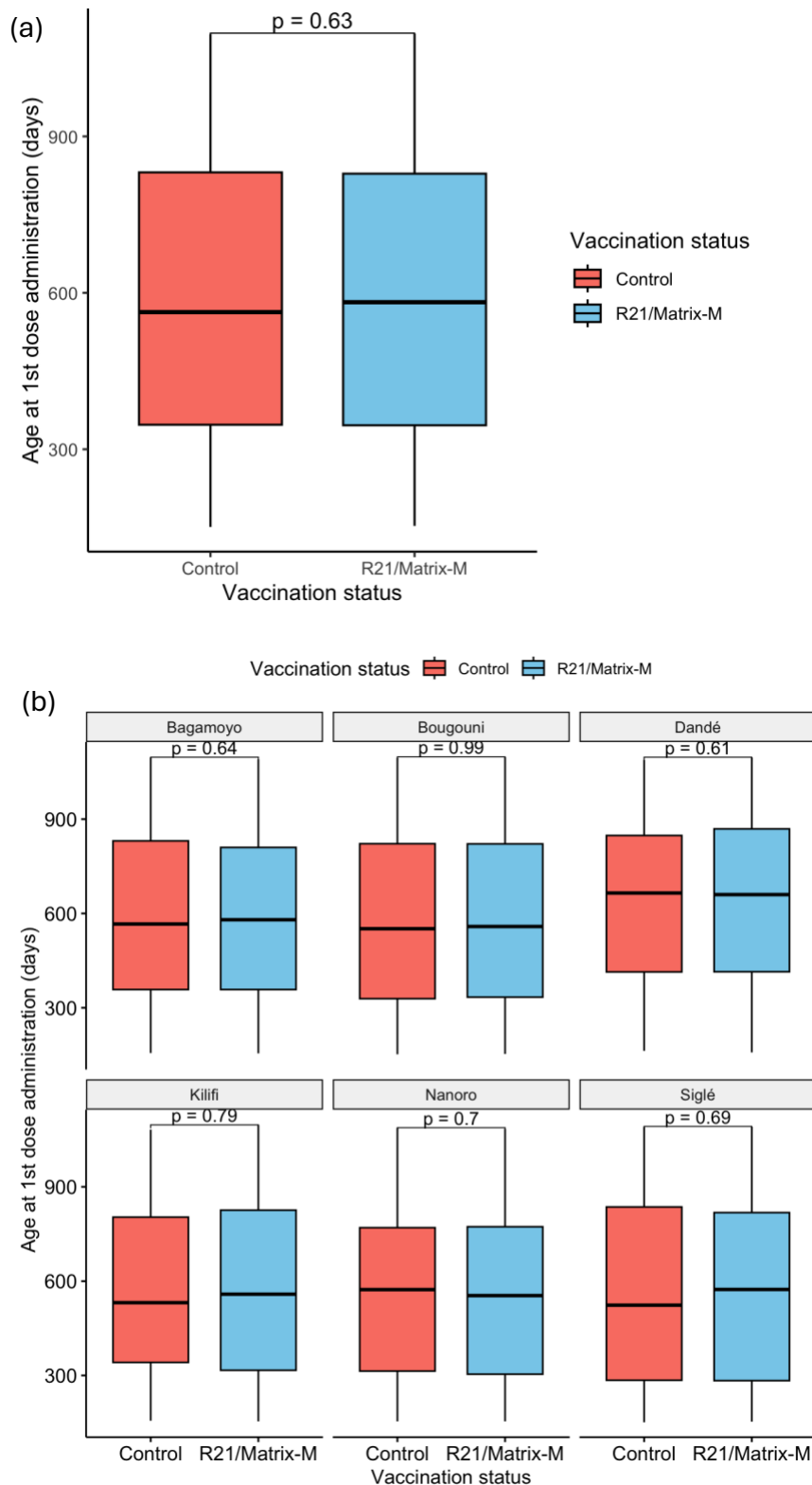


Figure.S1 Comparison of age distribution between vaccination groups.

Box plots show the distribution of age (in days) at the first primary series vaccine dose administration by vaccination group (Control vs R21/Matrix-M). **(a)** Comparison across all study sites combined. **(b)** Comparison stratified by individual study site. *p*-values were calculated using the Wilcoxon signed-rank test, which was chosen due to non-normal distribution of the data.

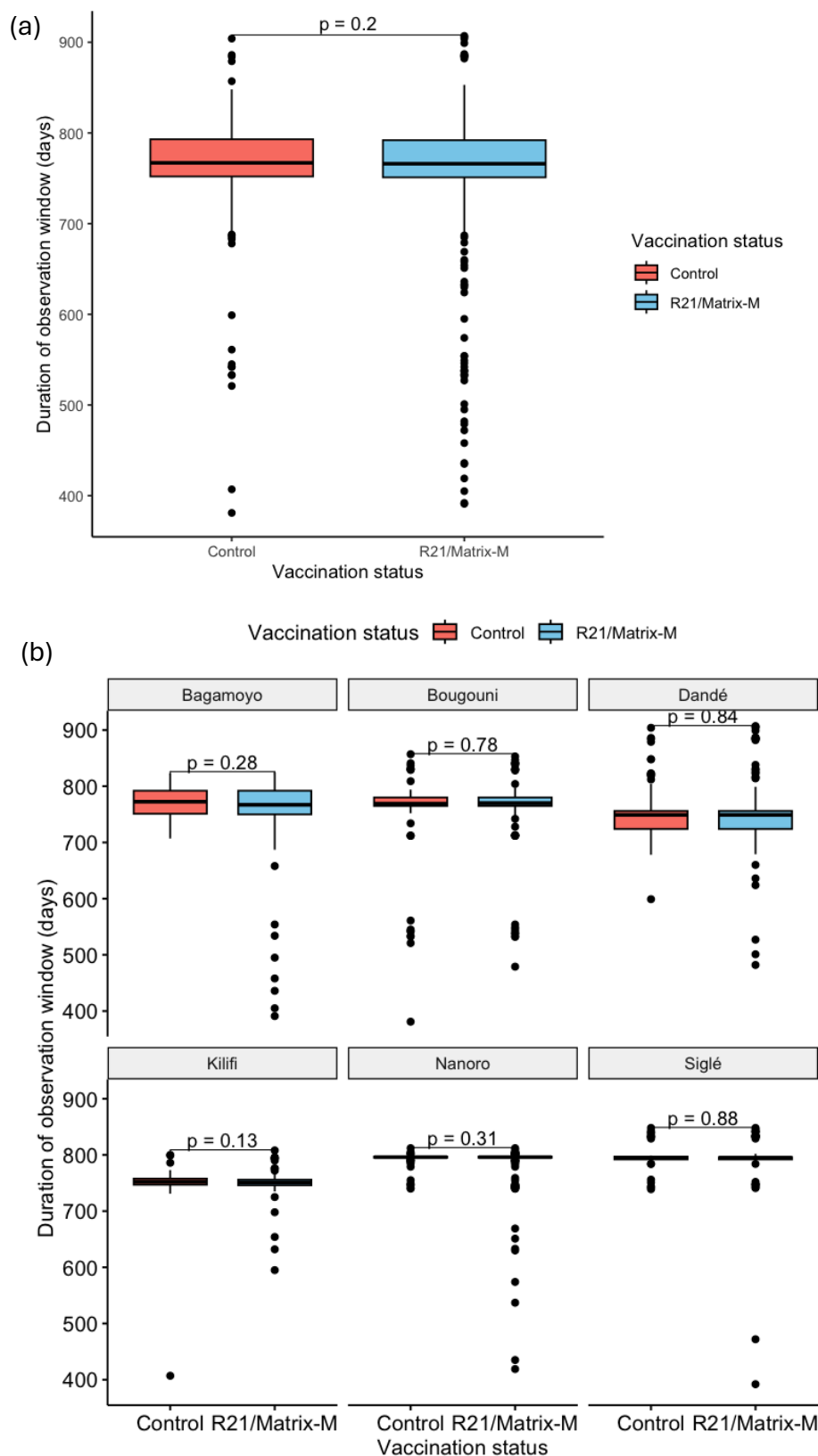


Figure.S2 Comparison of observation window duration between vaccination groups. Box plots show the distribution of observation window duration (in days) by vaccination group (Control vs R21/Matrix-M). **(a)** Comparison across all study sites combined. **(b)** Comparison stratified by individual study site. *p*-values were calculated using the Wilcoxon signed-rank test, which was chosen due to non-normal distribution of the data.

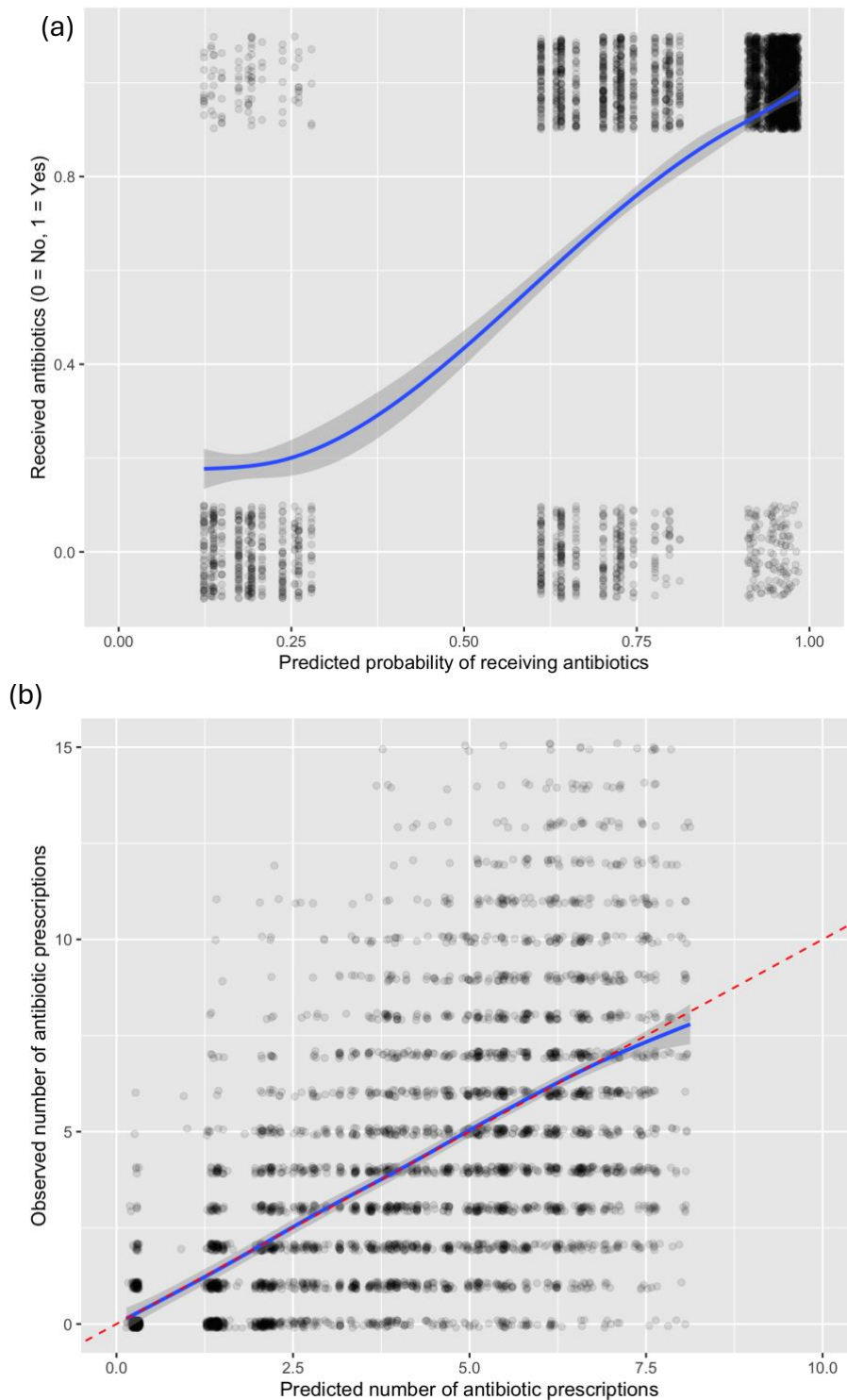


Figure.S3 Model diagnostic plots of generalised linear mixed models.

(a) Logistic regression model. **(b)** Negative binomial regression for rate model. Each point represents an individual observation data point. X-axis represents predicted probabilities or predicted number of antibiotic prescriptions from the models, and y-axis represents the actual observed outcomes in the data. Points are jittered vertically to reduce overplotting. The blue lines represent smoothed trends of the relationship between predictions and observations with 95% confidence intervals (grey shades). The red dashed line ($y=x$) indicates perfect model calibration where predictions exactly match observations.

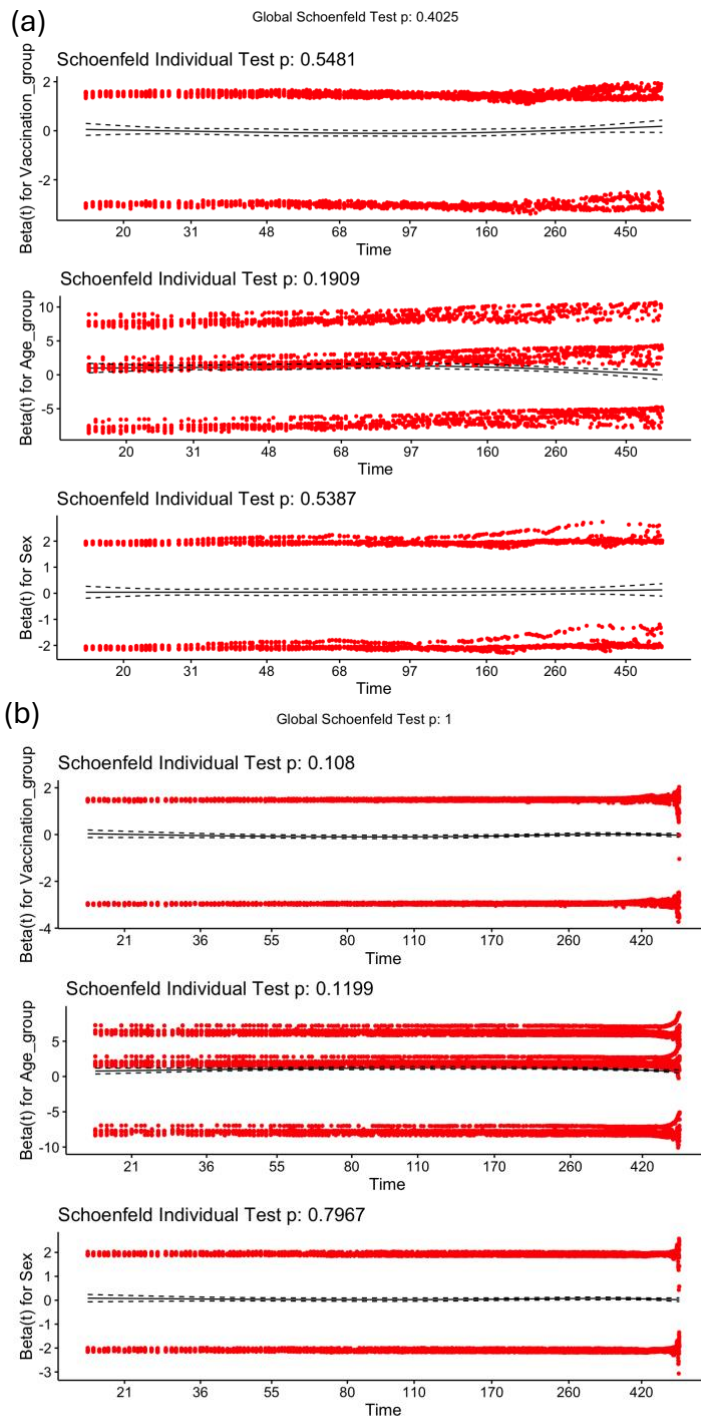


Figure.S4 Assessment of proportional hazards assumptions of Cox models using Schoenfeld residual analysis.

(a) Standard Cox proportional hazards model. **(b)** Recurrent event Andersen-Gill Cox model. Beta(t) indicates the estimated coefficient of the covariate effects on hazards over time. Red dots represent scaled Schoenfeld residuals, and black solid lines represent the smoothed trend lines with 95% confidence intervals (dashed). The null hypothesis was defined as proportional hazards assumptions being true. The horizontal trend and $p > 0.05$ suggested that the proportional hazards assumptions were not violated, and the effect of each covariate on antibiotic usage did not vary over time.

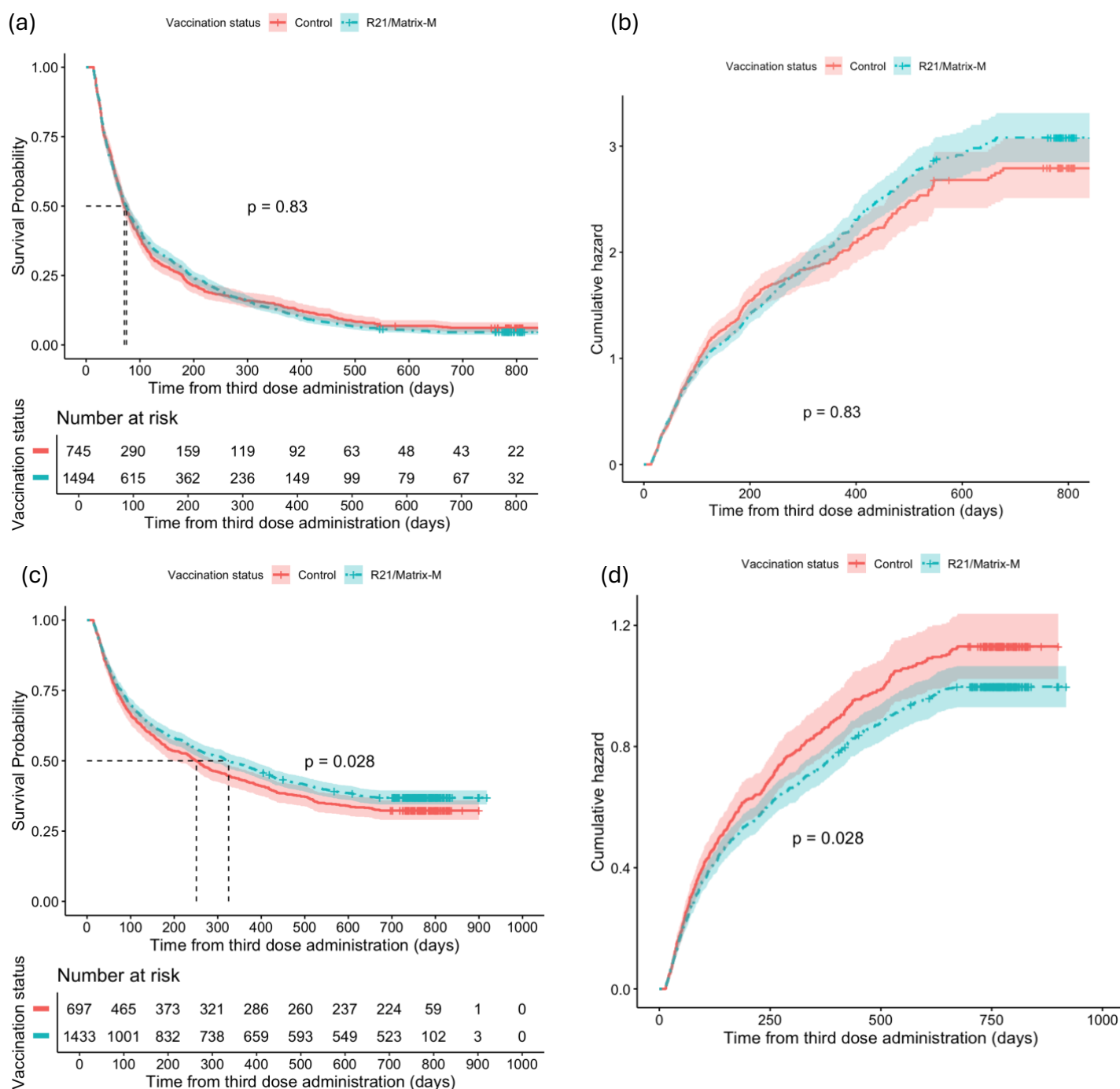


Figure.S5 Kaplan-Meier estimates of time to first antibiotic prescription by vaccination group, stratified by transmission setting (a,b: seasonal sites; c,d: perennial sites).

(a, c) Kaplan–Meier survival curves showing the probability of not receiving antibiotic prescription in the control and R21/Matrix-M groups. The number of individuals at risk at intervals of 100 days is shown in the risk table below the plot. **(b, d)** Cumulative hazard plot comparing the hazards of receiving an antibiotic prescription over time between vaccination groups. Time was calculated from the administration date of the third dose in the primary series vaccine. p -value was based on the log-rank test, comparing the survival times between two groups. Vertical bars on the curves represent censored individuals. Shades represent 95% confidence intervals. Dashed vertical and horizontal lines represent median survival.

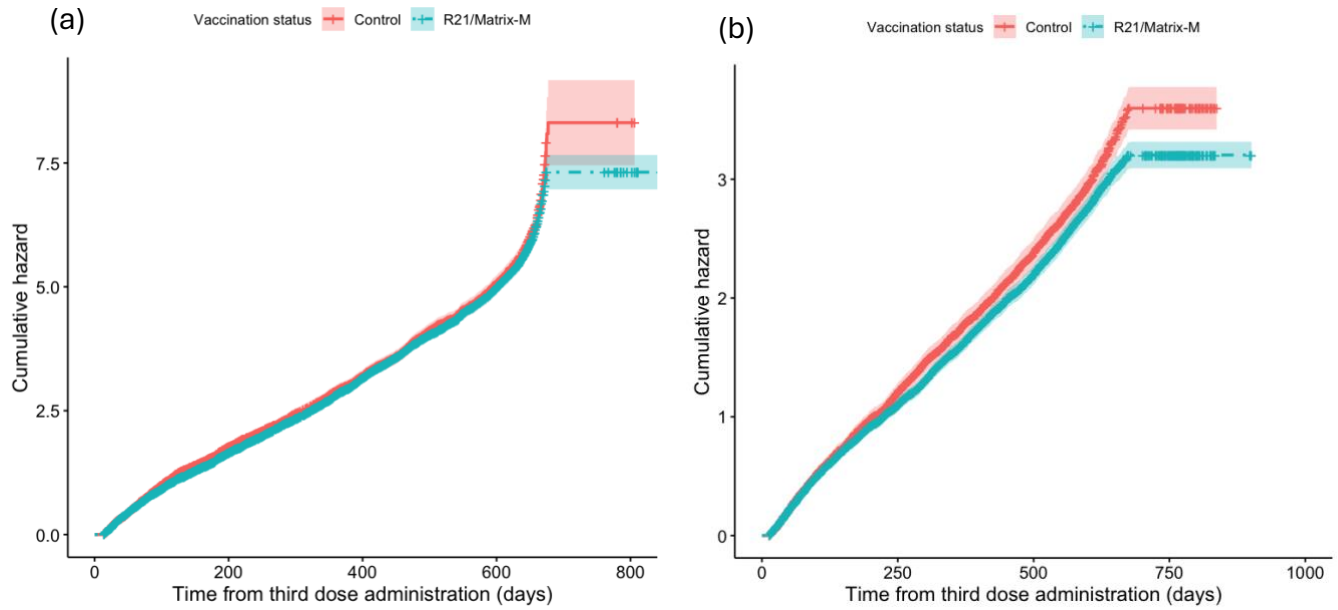
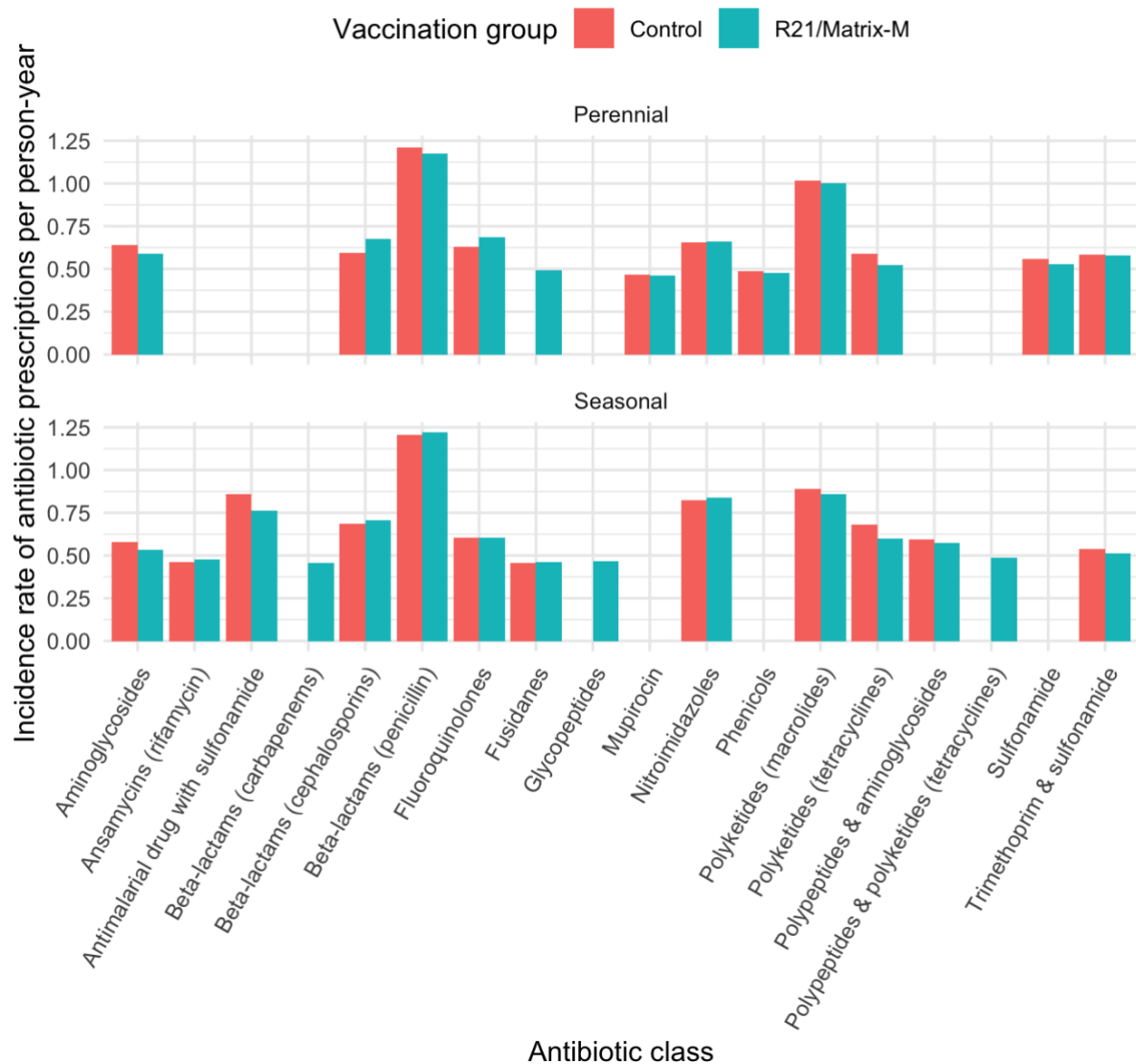


Figure.S6 Kaplan-Meier estimates of time to recurrent antibiotic prescriptions by vaccination group stratified by transmission setting (a: seasonal sites; b: perennial sites). Cumulative hazard plot comparing the hazards of receiving multiple repeated antibiotic prescriptions over time between vaccination groups. Time was calculated from the administration date of the third dose in the primary series vaccine. Vertical bars on the curves represent censored individuals. Shades represent 95% confidence intervals.

(a) Incidence rate of antibiotic prescriptions per person-year by antibiotic class and vaccination status



(b) Proportion of antibiotic prescriptions by antibiotic class and vaccination status

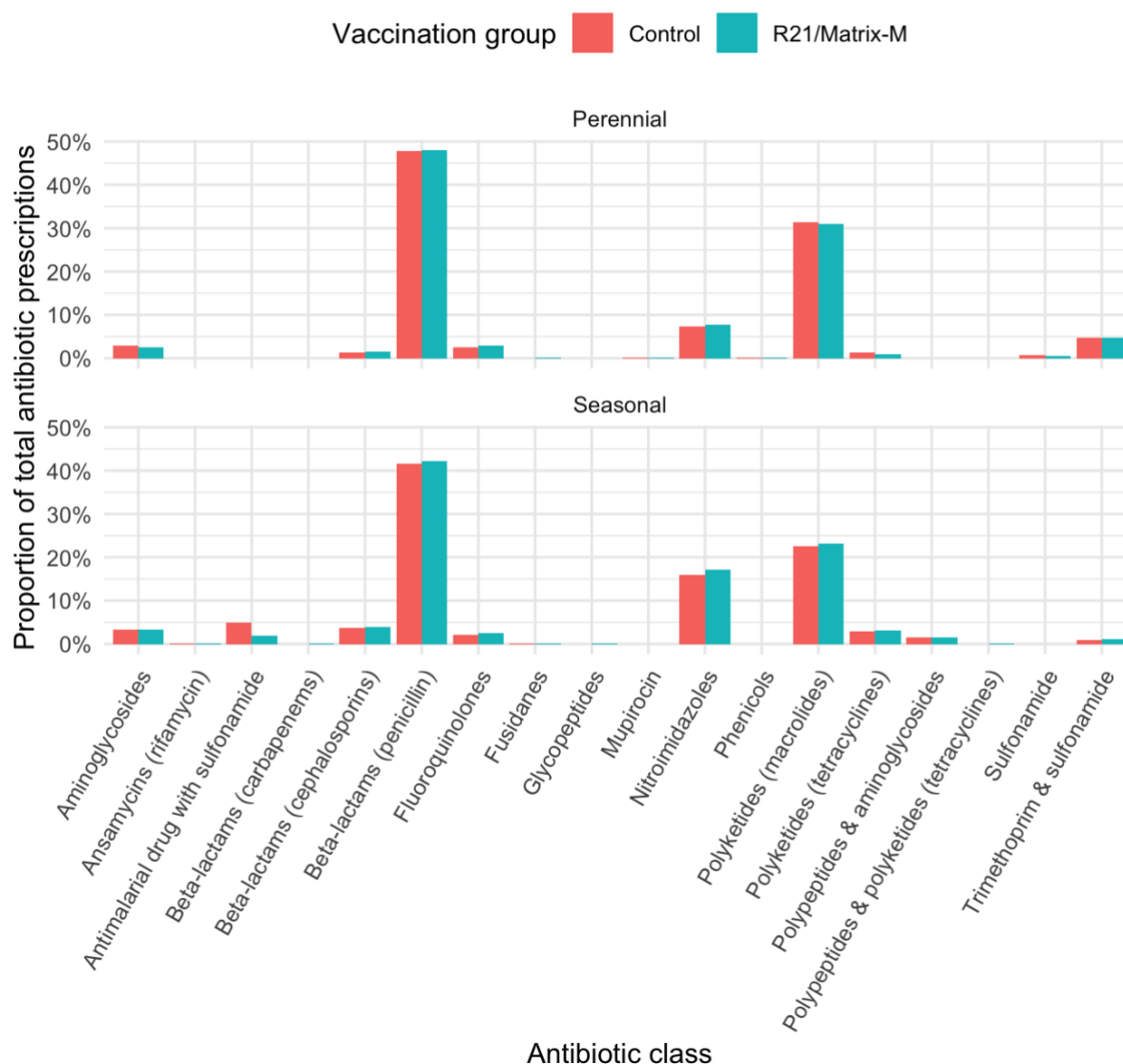
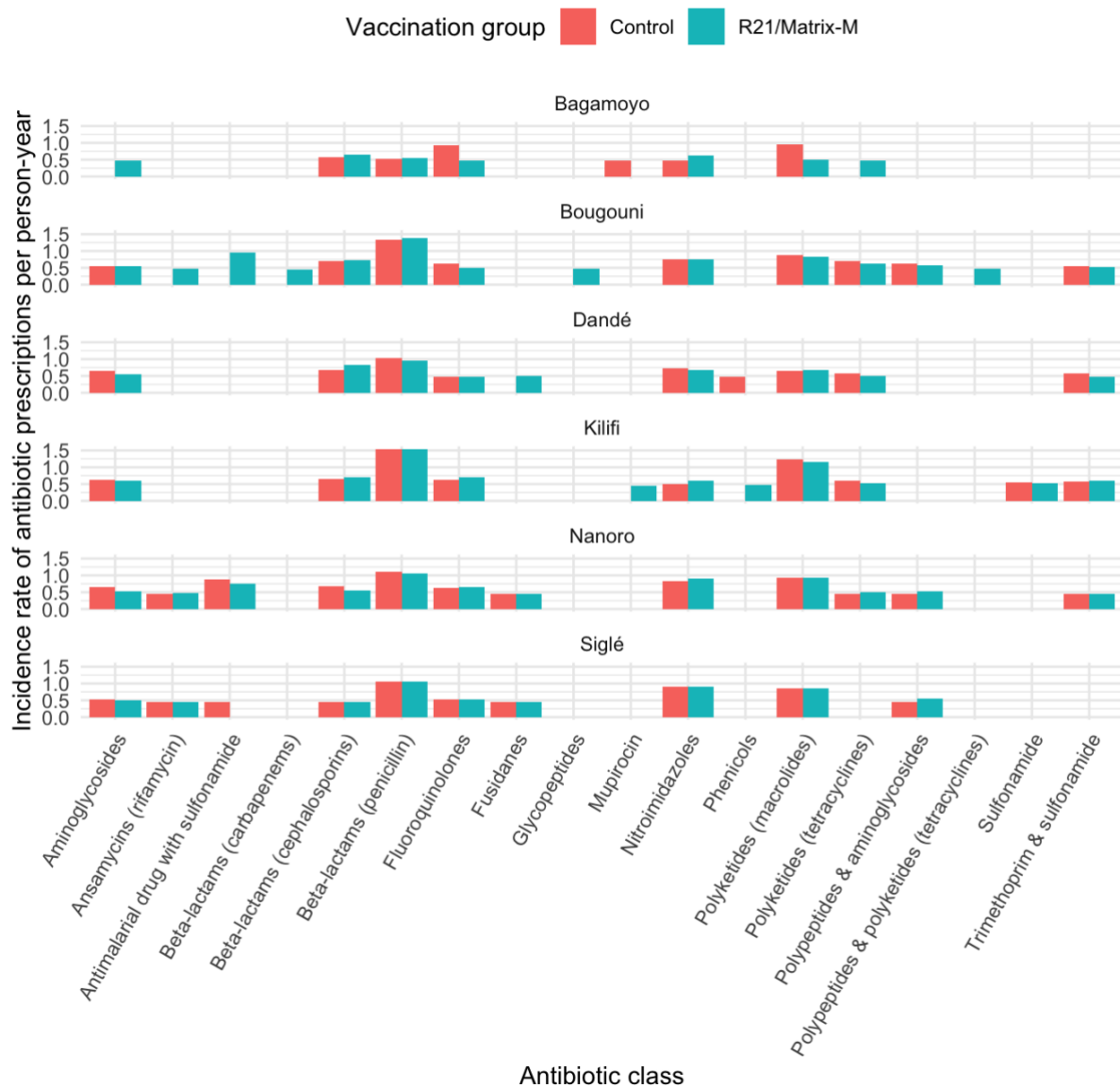


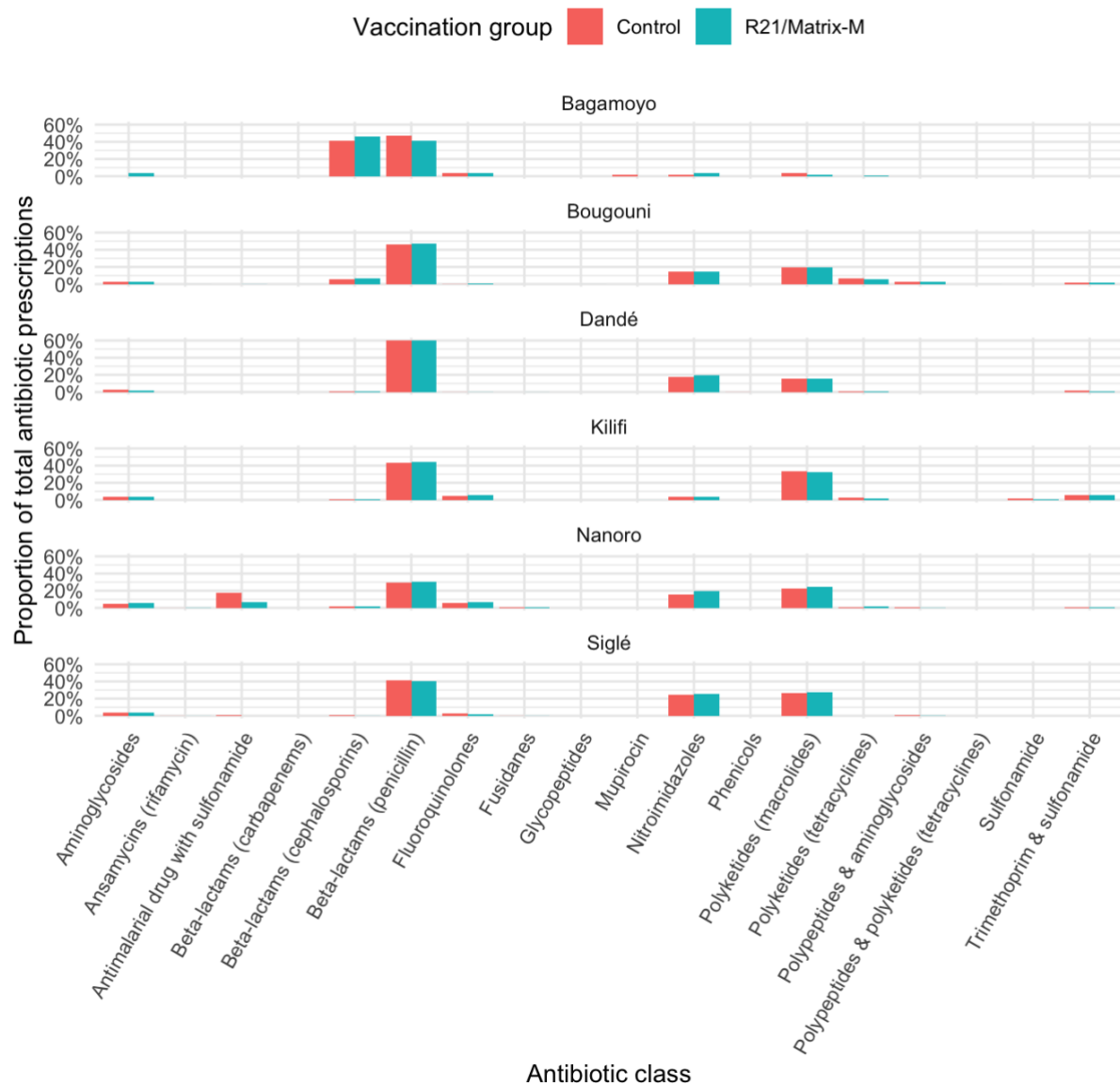
Figure.S7 Antibiotic prescriptions by antibiotic class and vaccination group, stratified by transmission setting.

(a) Incidence rate of antibiotic prescription per person-year of follow-up. (b) Proportion of total antibiotic prescriptions belonging to each class within the control and R21/Matrix-M groups. Classification details are provided in Table.S8.

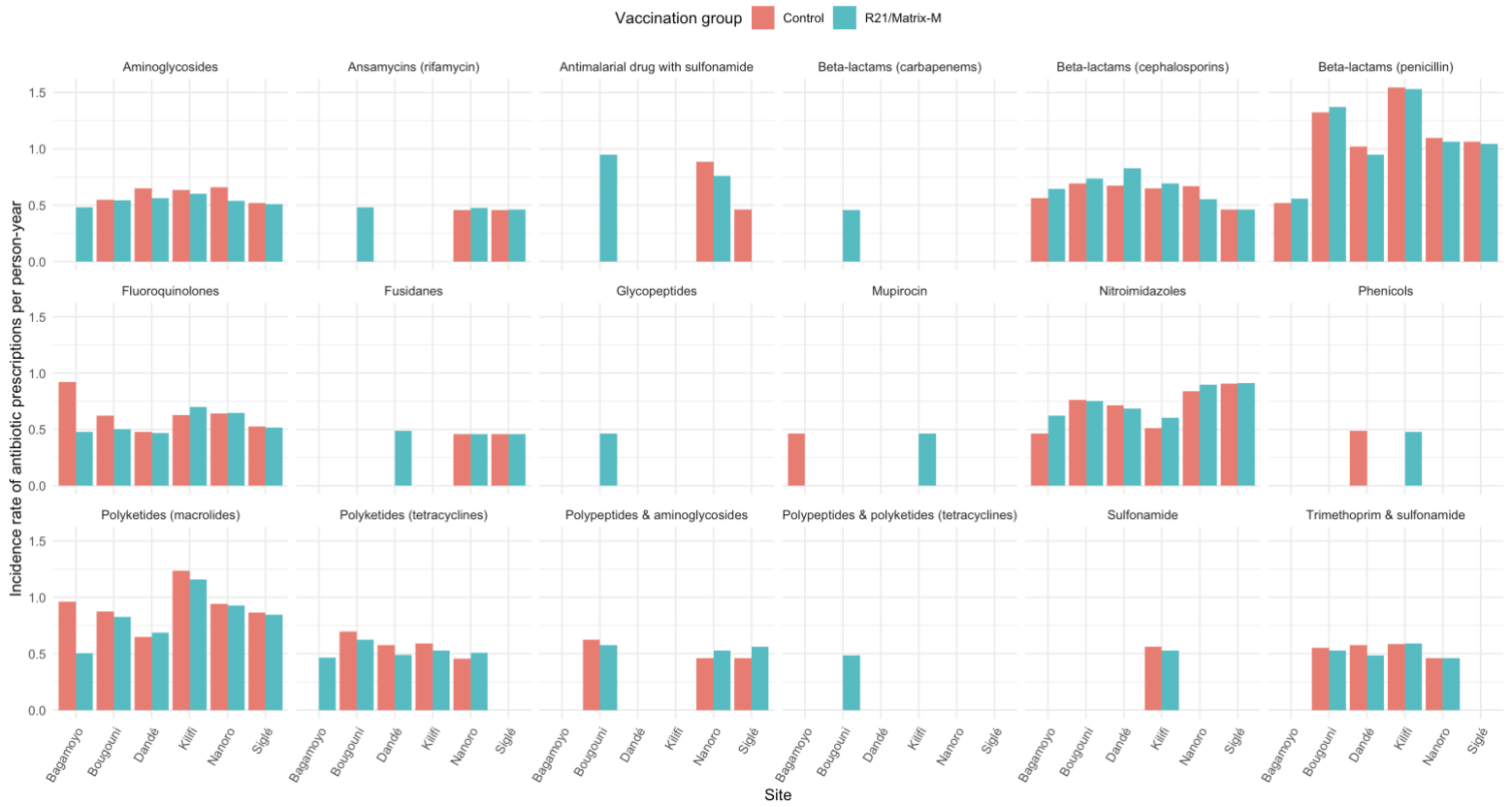
(a) Incidence rate of antibiotic prescriptions per person-year by antibiotic class and vaccination status



(b) Proportion of antibiotic prescriptions by antibiotic class and vaccination status



(C) Incidence rate of antibiotic prescriptions per person-year by antibiotic class and vaccination status



(d) Proportion of antibiotic prescriptions by antibiotic class and vaccination status

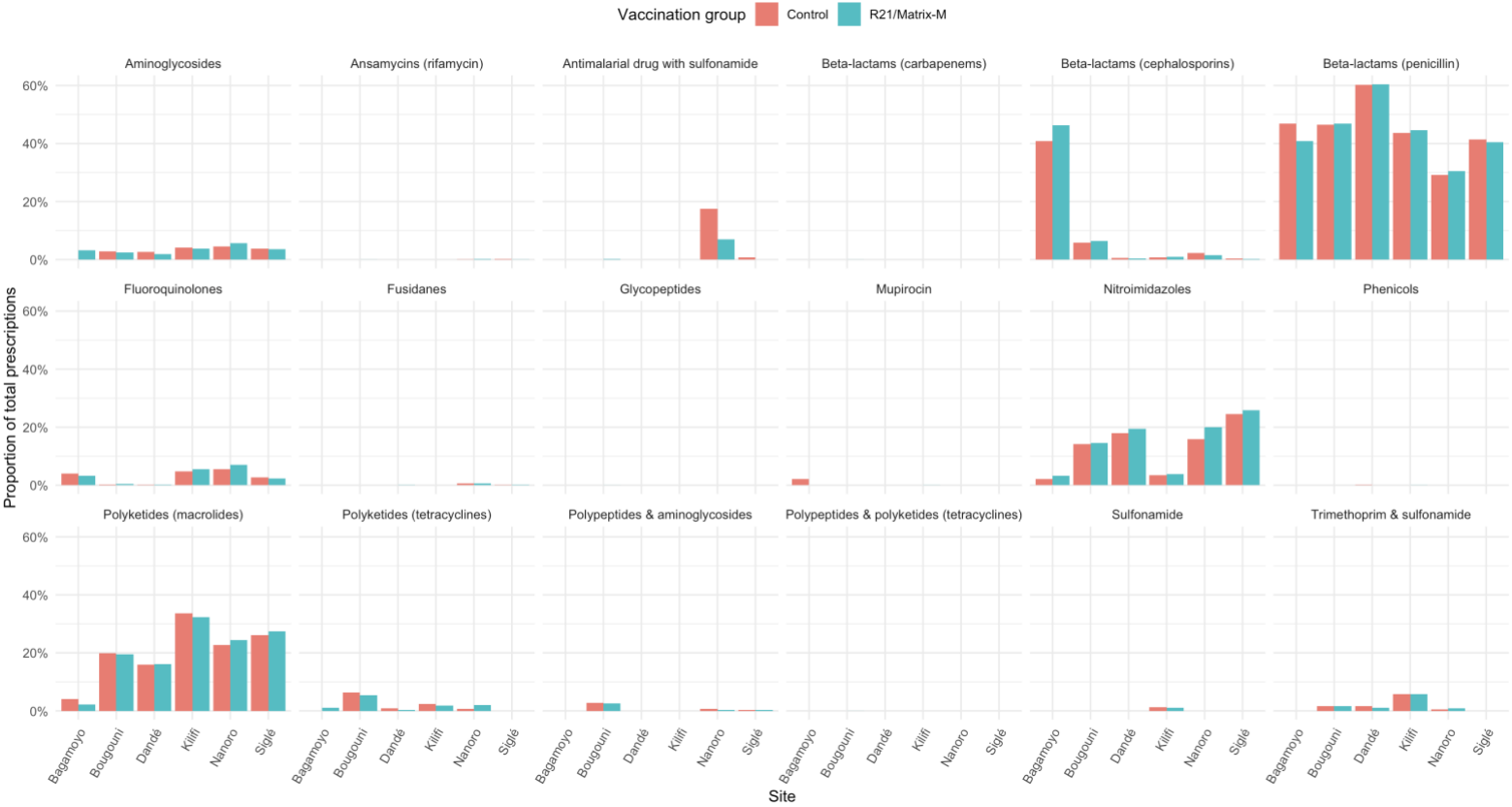


Figure.S8 Antibiotic prescriptions by antibiotic class and vaccination group, stratified by individual site.
(a, c) Incidence rate of antibiotic prescription per person-years of follow-up, faceted by (a) site and (c) antibiotic class. (b, d) Proportion of total antibiotic prescriptions belonging to each class within the control and R21/Matrix-M groups, faceted by (a) site and (c) antibiotic class. Classification details are provided in Table.S8.

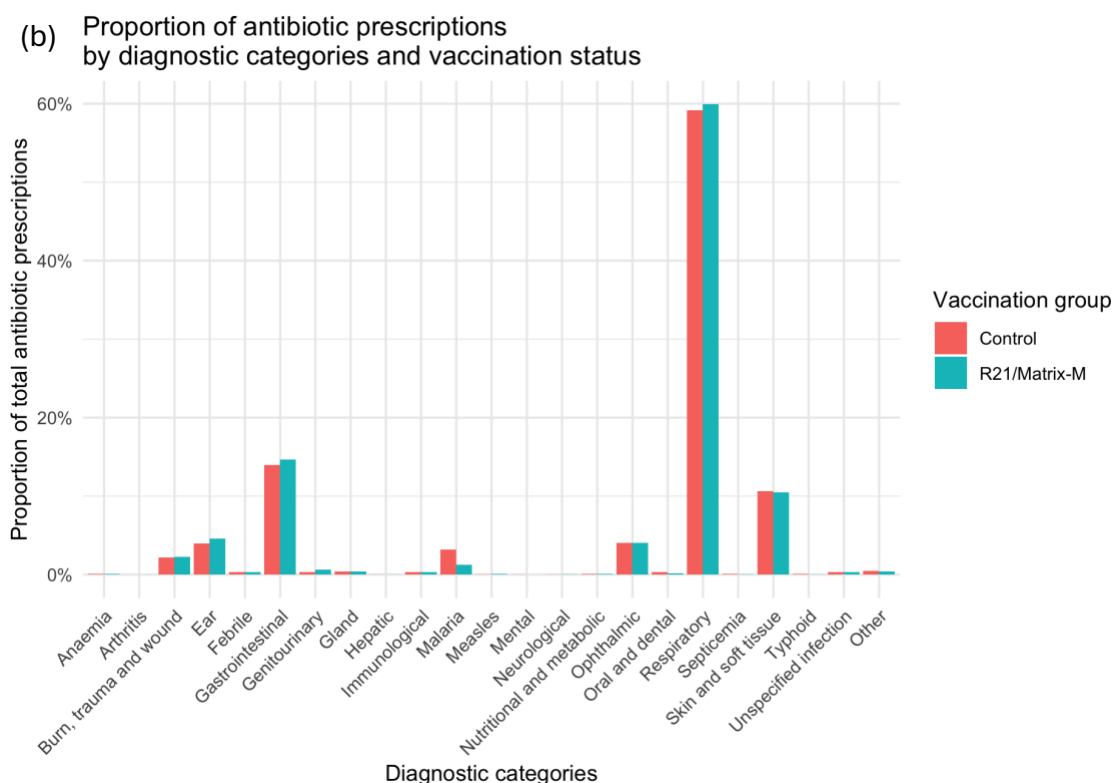
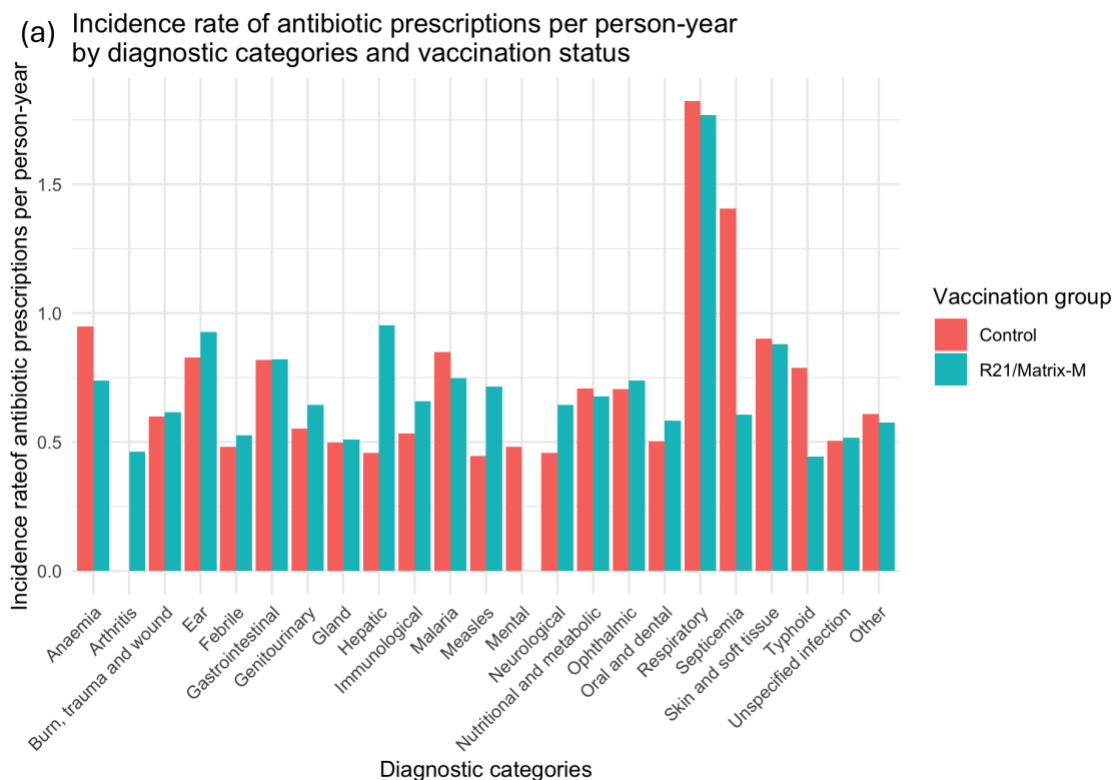
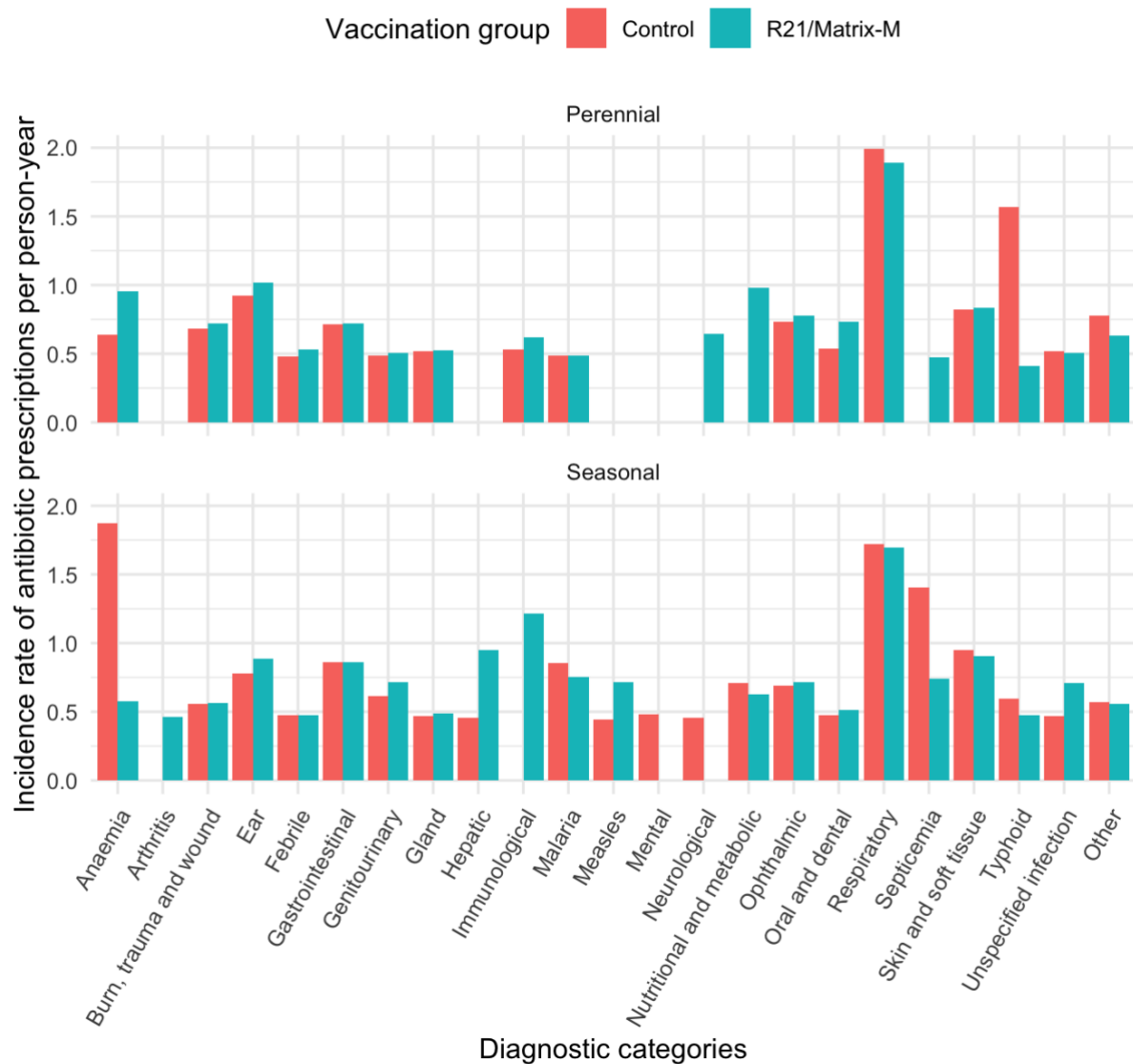


Figure.S9 Antibiotic prescriptions by diagnostic reason and vaccination group across all sites with detailed and granular classification.

(a) Incidence rate of antibiotic prescription per person-year of follow-up. **(b)** Proportion of total antibiotic prescriptions belonging to each diagnostic category within the control and R21/Matrix-M groups.

(a) Incidence rate of antibiotic prescriptions per person-year by diagnostic categories and vaccination status



(b) Proportion of antibiotic prescriptions by diagnostic categories and vaccination status

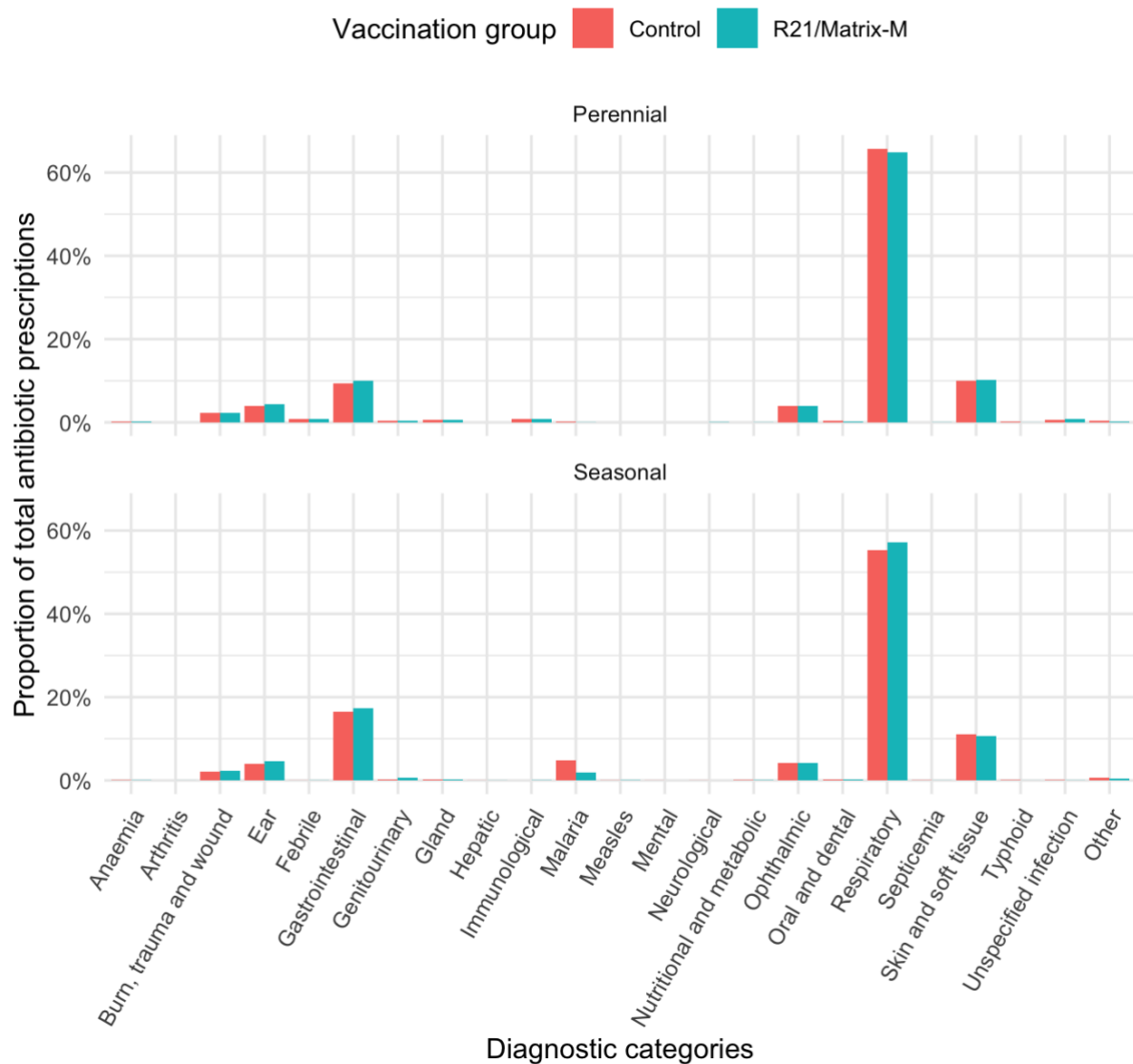
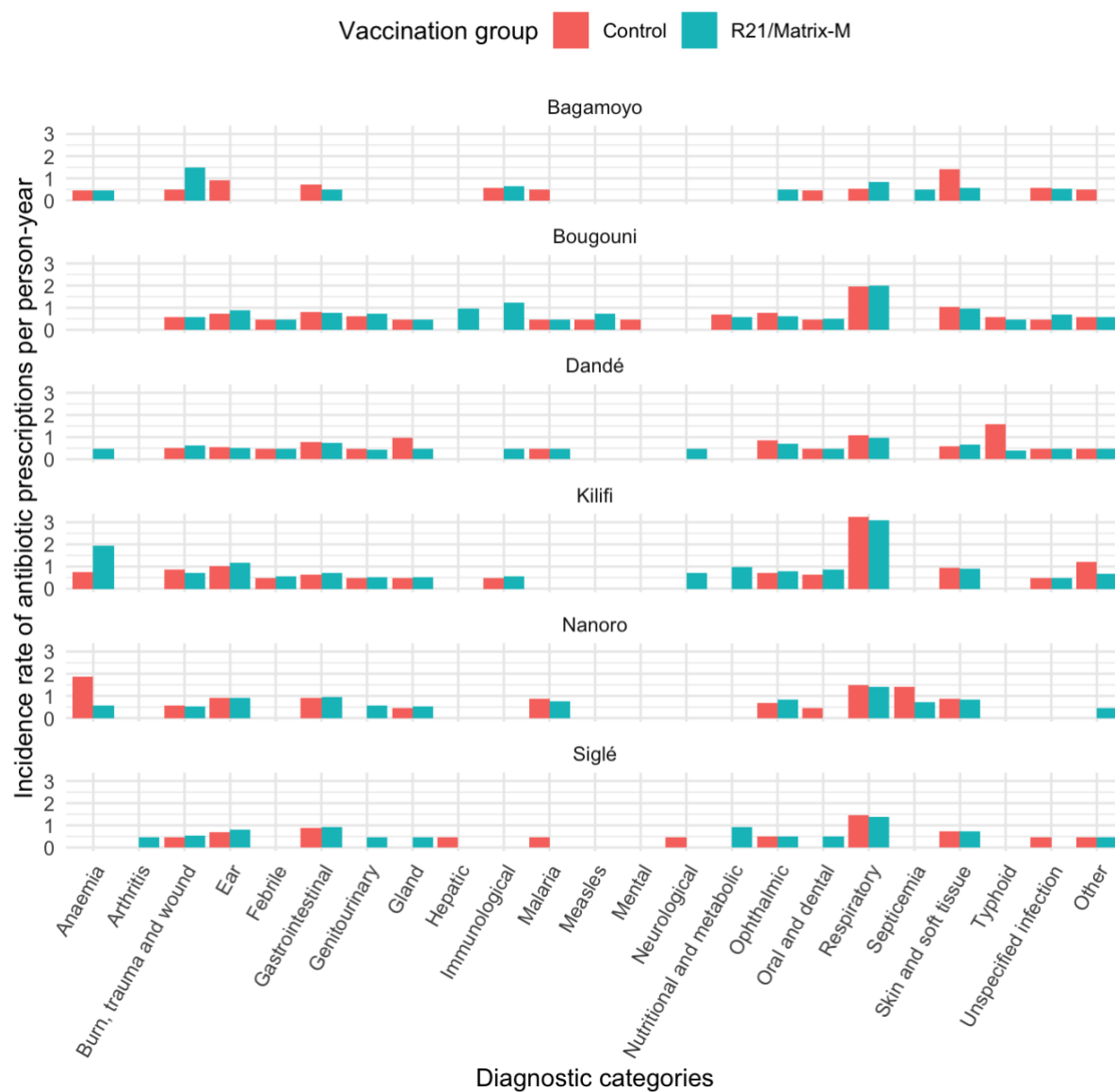


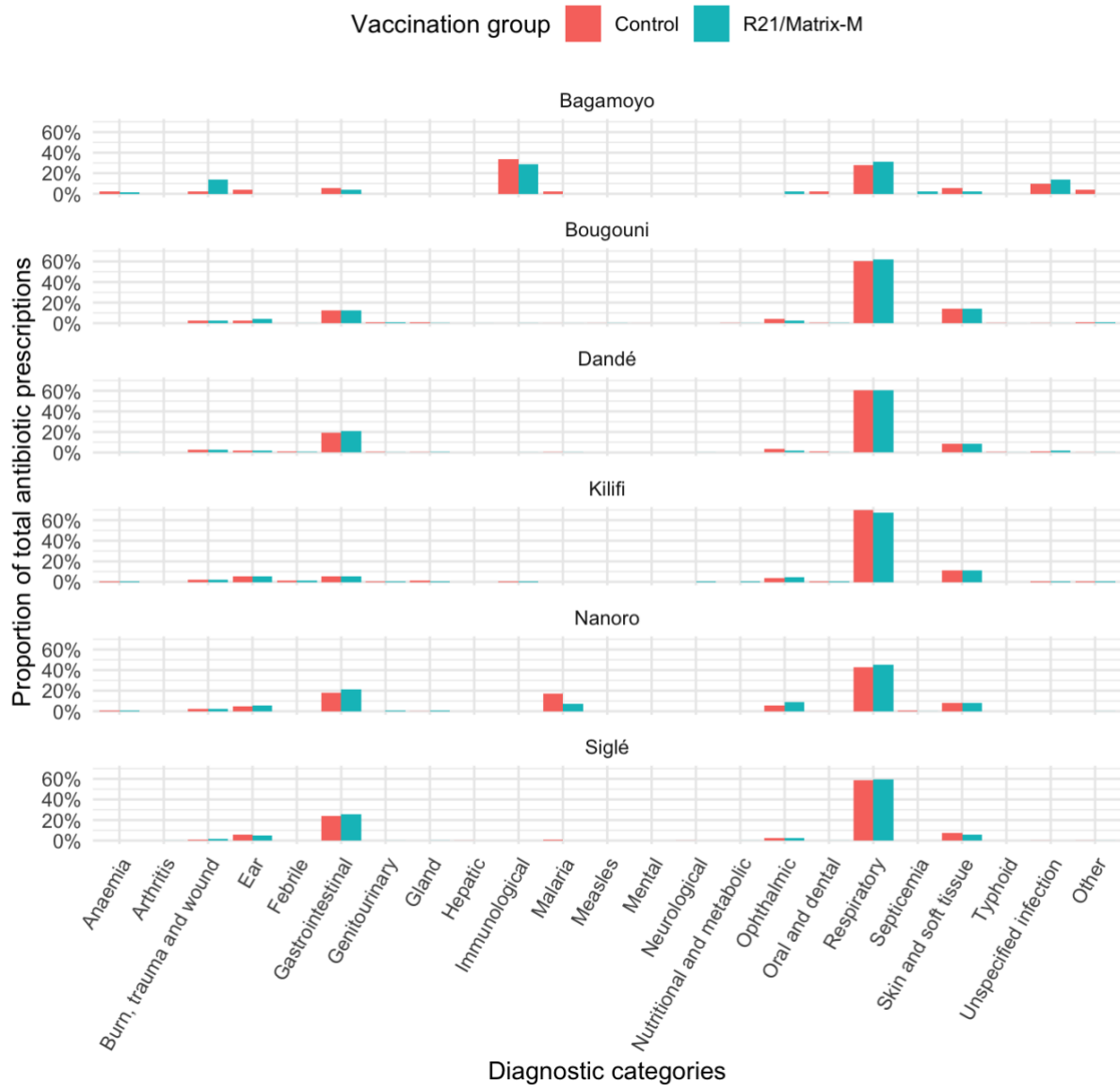
Figure.S10 Antibiotic prescriptions by diagnostic reason and vaccination group with detailed and granular classification, stratified by transmission setting.

(a) Incidence rate of antibiotic prescription per person-year of follow-up. (b) Proportion of total antibiotic prescriptions belonging to each diagnostic category within the control and R21/Matrix-M groups.

(a) Incidence rate of antibiotic prescriptions per person-year by diagnostic categories and vaccination status



(b) Proportion of antibiotic prescriptions by diagnostic categories and vaccination status



(c) Incidence rate of antibiotic prescriptions per person-year by diagnostic categories and vaccination status



(d) Proportion of antibiotic prescriptions by diagnostic categories and vaccination status



Figure.S11 Antibiotic prescriptions by diagnostic reason and vaccination group with detailed and granular classification, stratified by individual site.

(a, c) Incidence rate of antibiotic prescription per person-year of follow-up, faceted by (a) site and (c) diagnostic category. (b, d) Proportion of total antibiotic prescriptions belonging to each diagnostic category within the control and R21/Matrix-M groups, faceted by (a) site and (c) diagnostic category.