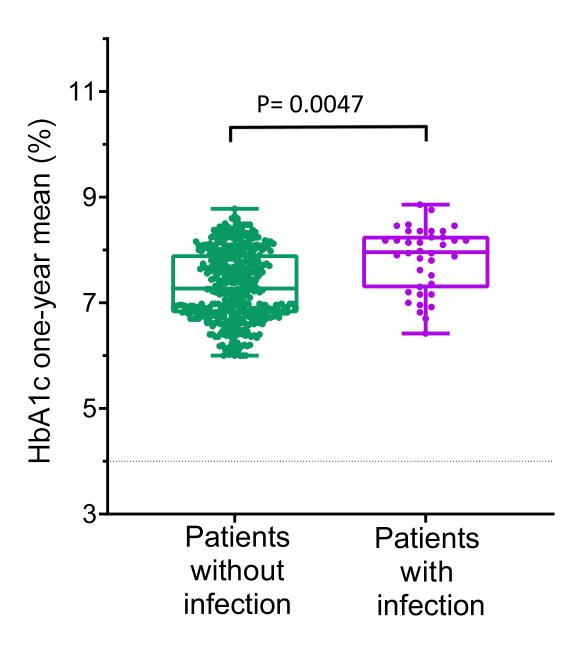
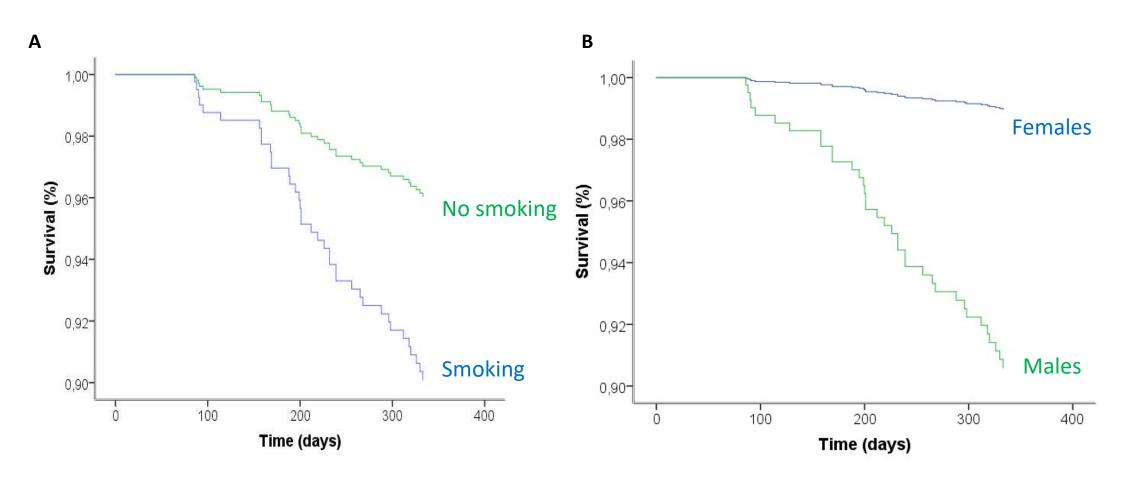


Supplementary Figure 1. Levels of the one-year mean of HbA1c in subjects with or without infections during the follow-up. The one year mean of HbA1c in patients without infection (n=456) and in patients with infection (n=38). Boxplots show the median, 25th, and 75th percentiles, range, and extreme values. P derives from two-tailed Student's t test.

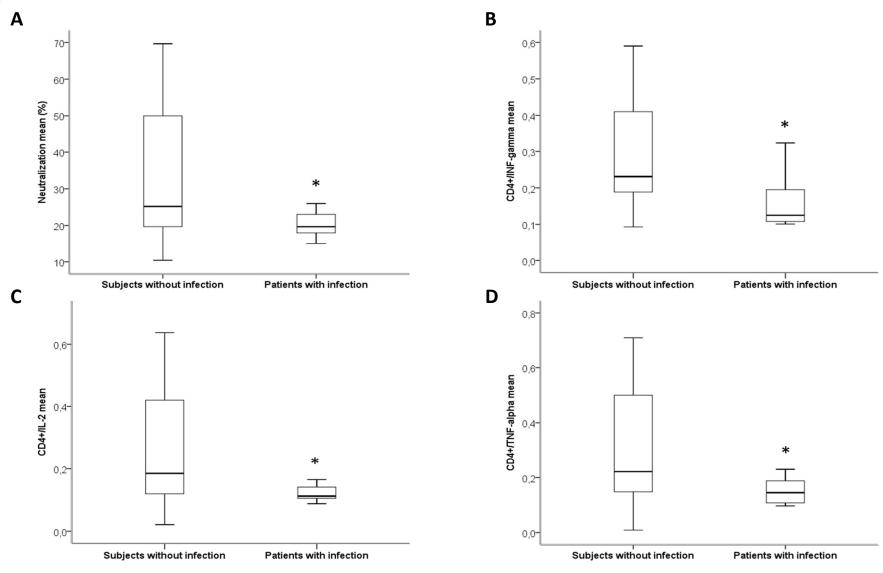


Supplementary Figure 2. Effect of smoking (A) and sex (B) on the development of breakthrough infections.

Standardized cumulative incidence of infections comparing smokers vs no-smokers (A) and males vs females (B).



Supplementary Figure 3. Immune-related parameters in subjects with or without infections during the follow-up. The mean of neutralizing antibodies capacity (assessed as percentage of neutralization) ( $\mathbf{A}$ ), the proportion of CD4+ T cells producing interferon- $\gamma$  (IFN $\gamma$ ) ( $\mathbf{B}$ ), interleukin-2 (IL-2) ( $\mathbf{C}$ ), and tumor necrosis factor-  $\alpha$  (TNF- $\alpha$ ) ( $\mathbf{D}$ ), in subjects without infection (one-year mean, 5 evaluations, n=456), and in patients with infection (mean before infection, 3±2 evaluations, n=38). Boxplots show the median, 25th, and 75th percentiles, range, and extreme values. \*P<0.01 Two-tailed Student's t test with Bonferroni correction.



## Supplementary Figure 4. Example of the gating strategy used for cytofluorimetric experiments.

