

Response to: 'Emergency arising from patients' fear of taking antimalarials during these COVID-19 times: are antimalarials as unsafe for cardiovascular health as recent reports suggest?' by Santos-Moreno *et al*

We thank Santos-Moreno *et al* for their response to our commentary.^{1,2} The authors provide data on cardiovascular adverse events associated with maintenance antimalarial use for patients with rheumatoid arthritis (RA). In addition to our previous correspondence response³ from Erre *et al*,⁴ these additional data are reassuring to patients with rheumatic diseases on chronic doses of antimalarials regarding the continued safety of these medications.

However, as we have also addressed in a previous response, the safety profile of antimalarials in patients with COVID-19 infection compared with patients with rheumatic disease may differ widely. Observational data regarding cardiovascular events in hospitalised patients with COVID-19 treated with hydroxychloroquine (HCQ) with or without azithromycin have found variable rates of QTc prolongation and arrhythmias.⁵⁻⁷ Lane *et al* recently used combined electronic health record and administrative data from five countries and a new user, active comparator cohort design to address two scientific questions among adults with RA:⁸ (1) the risk of serious adverse events, particularly cardiovascular events, among individuals with RA initiating therapy with HCQ versus sulfasalazine; (2) the risk of these outcomes when azithromycin is started (compared with starting amoxicillin) among prevalent HCQ users with RA. The cardiovascular outcomes assessed in that study included cardiovascular mortality, cardiac arrhythmia, and heart failure, and were identified using ICD codes.⁸ However, there was no statistically significant association between HCQ use and cardiac arrhythmia, compared with sulfasalazine use (calibrated HR 0.89, 95% CI 0.77 to 1.04) among individuals with RA.⁸ Although a similarly designed study using population-level data could be conceived to assess the study question presented by Santos-Moreno *et al*, the surrogate outcome of QTc prolongation would be more difficult to ascertain using administrative/claims data.

In summary, we agree that these data offer additional support that the possible cardiotoxicity of antimalarials for treatment of COVID-19 should not be extrapolated to patients with rheumatic disease where its safety and efficacy is well established.

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