

**Baseline retinal testing is no longer recommended for  
hydroxychloroquine users in the United Kingdom**

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# Baseline retinal testing is no longer recommended for hydroxychloroquine users in the United Kingdom

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The revised BSR DMARD guidelines introduced substantial changes to monitoring recommendations for Hydroxychloroquine.<sup>1</sup> The guidelines, which reflected the Royal College of Ophthalmologists (RCOphth) 2018 recommendations on retinal monitoring,<sup>2</sup> introduced a significant burden on clinical teams, and some services were unable to deliver them. The RCOphth has now published updated guidelines on retinal monitoring for hydroxychloroquine and chloroquine users in the United Kingdom (December 2020).<sup>3</sup> The revised guidelines should be welcomed by patients, rheumatologists and ophthalmologists. This editorial summarises the key changes to the recommendations which will impact on the clinical practice of rheumatologists and other prescribers of hydroxychloroquine.

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The new RCOphth recommendations do not support baseline testing for initiators of hydroxychloroquine and chloroquine. Annual retinal monitoring should begin after 1 year of treatment initiation if additional risk factors for retinal toxicity are present, and after 5 years for all other users (**Figure 1**). Additional risk factors include a high-dose of hydroxychloroquine (>5mg/kg per day), concurrent tamoxifen use, renal impairment (eGFR <60ml/min/1.73m<sup>2</sup>) and chloroquine use.<sup>4, 5</sup> At monitoring visits, it is recommended that all users undergo retinal imaging with optical coherence tomography and fundus autofluorescence imaging. Visual field testing - which is time-consuming and often unreliable<sup>6, 7</sup> - should be used only as a second line test (**Figure 1**).

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The new RCOphth recommendations are expected to increase the efficiency and reduce the cost<sup>7</sup> of delivering monitoring services without reducing the overall diagnostic yield. Virtual clinics in which a patient undergoes retinal imaging tests which are reviewed by a clinician at a later time are better suited to the new monitoring algorithm. The reduced cost of monitoring should facilitate Clinical Commissioning Groups to fund services and protect hydroxychloroquine users and prescribers. Concerns about the effectiveness of baseline testing and the incomplete coverage of monitoring services highlighted in the British Society for Rheumatology's statement on retinal monitoring for hydroxychloroquine and chloroquine users<sup>8</sup> (30<sup>th</sup> March 2020) are in part addressed by the new recommendations.

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A review of the RCOphth guideline (2018)<sup>2</sup> was prompted by the publication of additional studies judged to be of sufficient quality and relevance. The literature was systematically evaluated to identify studies relevant to the timing of monitoring and the tests that should be performed; the full methodology is detailed in the published guideline.<sup>9</sup> In particular, two

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high-quality published audits of hydroxychloroquine retinopathy monitoring services undertaken according to the 2018 recommendations were identified.<sup>6, 7</sup> Marshall *et al* identified that of 782 individuals who received a baseline assessment (mean duration of therapy: 1.7 years, SD 1.3 years), none were found to have abnormalities which precluded continued use of hydroxychloroquine.<sup>6</sup> Gobbett *et al* found that of 345 baseline assessment visits, only 26 individuals were unsuitable for monitoring due to co-existing pathologies (pooled frequency of abnormalities on baseline testing: 2.3% across both studies).

Baseline testing was found to account for over half of all monitoring visits overall, involving the use of significant resources.<sup>7</sup> Furthermore, it is recognised that a significant proportion of hydroxychloroquine initiators will no longer be taking the drug at 5 years due to intolerance or insufficient clinical response. On consideration of these data, the RCOphth guideline development group did not consider the limited clinical benefit of baseline testing to be sufficient to justify the significant resources required to support it.

A large case-control study had identified a prevalence of retinopathy of 7.5% in long-term (>5 years) hydroxychloroquine users in the U.S. using modern retinal imaging techniques.<sup>5</sup> However, this had not been replicated in other populations. Using the same diagnostic criteria, a prevalence of retinopathy of 6.3% in long-term hydroxychloroquine users was identified in a U.K. population, a difference that is likely explained by a disparity in risk characteristics between the groups.<sup>6</sup> This study further validated the case for retinal monitoring in the U.K.<sup>6</sup>

The same two studies identified visual field testing as a source of inefficiency in the monitoring protocol: 33.1% of tests were considered unreliable and 24.9% were of poor quality in one study<sup>6</sup> and 17% were unreliable in the other.<sup>7</sup> Further appointments are needed to repeat visual field tests due to poor reliability, poor quality or to ensure that any possible abnormality consistent with toxicity is repeatable.<sup>6</sup> Indeed, resources may be insufficient to repeat every visual field test.<sup>7</sup> The new RCOphth recommendations will reduce

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the inefficiency in the monitoring protocol attributed to visual field testing, which is now recommended only for individuals with objective retinal imaging abnormalities consistent with hydroxychloroquine retinopathy. The U.K. recommendations<sup>3</sup> on monitoring for hydroxychloroquine users now depart significantly from the current U.S. recommendations (2016) on baseline assessments and visual field testing.<sup>10</sup> However, improvements in the efficiency and cost-effectiveness of the monitoring protocol are expected to improve access to monitoring for individuals at risk of sight loss.

Rheumatologists should be aware of the new RCOphth recommendations for retinal monitoring in hydroxychloroquine and chloroquine users as summarised above, which should reduce the risk both for the user and prescriber. The Macular Society, in collaboration with the RCOphth, has produced an updated patient information leaflet which reflects the new guideline, available at [www.macularsociety.org](http://www.macularsociety.org).

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#### Key words

Hydroxychloroquine retinopathy; retinopathy; monitoring; screening; chloroquine;  
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Figure legends

Figure 1. Hydroxychloroquine retinopathy monitoring algorithm. Two abnormal test results are required for the diagnosis of hydroxychloroquine retinopathy. SD-OCT - spectral-domain optical coherence tomography; FAF – fundus autofluorescence imaging; ERG – electroretinography

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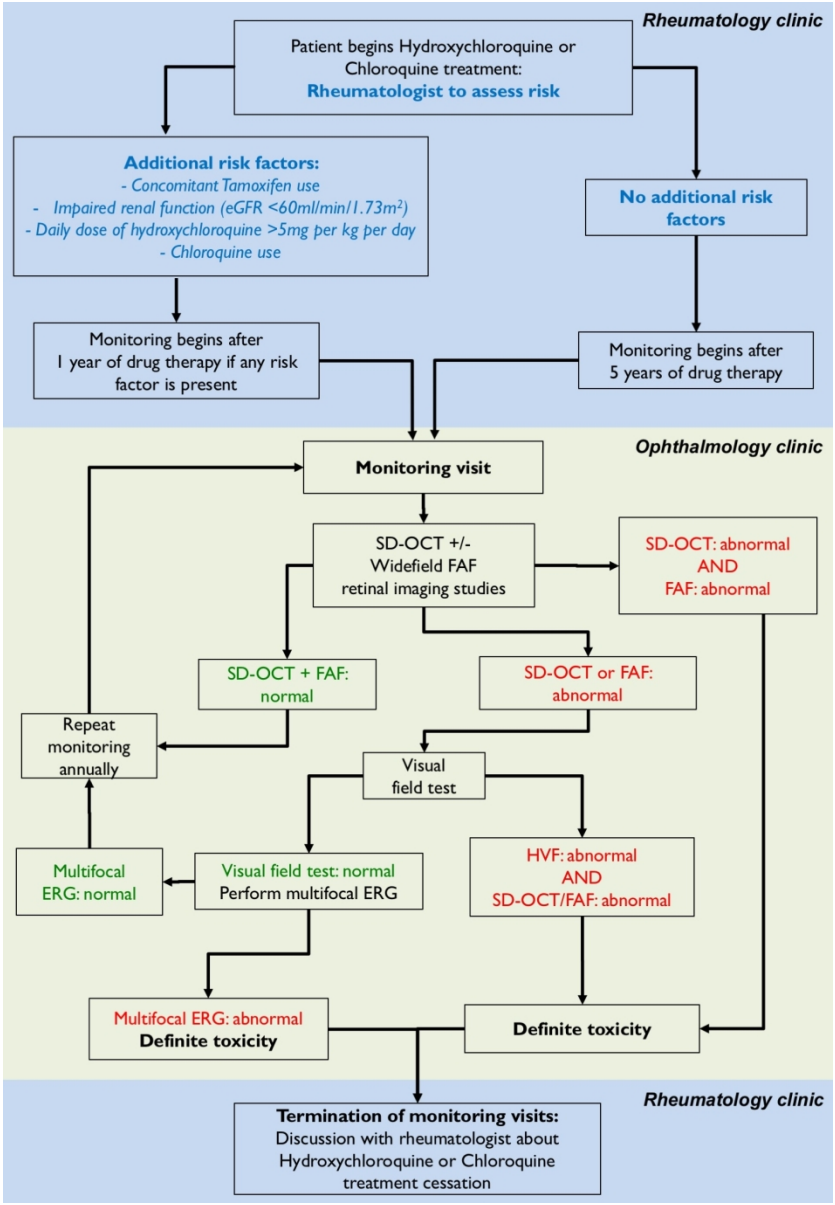


Figure 1. Hydroxychloroquine retinopathy monitoring algorithm.

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