

Real-World Performance of the 2020 RCOphth Imaging-Led Hydroxychloroquine Retinopathy Screening Pathway:

A Five-Year Virtual Clinic Analysis of 505 Patients

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INTRODUCTION

Hydroxychloroquine (HCQ) retinopathy is a preventable yet irreversible form of retinal toxicity whose true prevalence has become increasingly apparent with widespread adoption of multimodal imaging.

Prolonged therapy duration, high daily dosing, renal impairment and concurrent tamoxifen use substantially elevate toxicity risk.

2020 RCOphth Guideline Changes

In December 2020, the RCOphth introduced major revisions to the national HCQ monitoring guideline:

- Removed mandatory baseline ophthalmic screening
- Established an imaging-led approach with SD-OCT and widefield FAF as primary diagnostic tools
- Reserved visual field (VF) testing only for cases demonstrating structural abnormalities

This was a major shift from the 2018 guideline, which mandated annual OCT, FAF and VF for all eligible patients.

Study Aim

To evaluate real-world outcomes following implementation of the 2020 RCOphth guideline within a large virtual HCQ screening service, assessing:

- Demographic characteristics
- Systemic risk factors and treatment indications
- Imaging-based diagnostic yield
- Pathway-related delays
- Comparison with cohorts screened under the 2018 guideline

Why This Matters

HCQ is widely prescribed for rheumatological and dermatological conditions. Retinal toxicity from HCQ is dose- and duration-dependent, and once established it is irreversible.

Early detection through structured screening is therefore critical to preventing permanent visual loss.

The shift from a protocol requiring annual visual fields for all patients to a structure-led approach represents a significant change in clinical practice — with implications for diagnostic yield, resource use, and patient outcomes.

This study provides the first large-scale real-world evaluation of the 2020 pathway, offering important insights for centres adopting or planning to adopt the updated guideline.

METHODS

Retrospective study of 505 patients attending the hydroxychloroquine virtual screening clinic between January 2021 and December 2025.

Data Recorded

- Demographic features (age, sex)
- HCQ indication and therapy duration
- Daily dosing — alternate-day regimens standardised to 300 mg/day
- Renal function (eGFR)
- Tamoxifen co-exposure
- Referral source (GP, rheumatology, dermatology)
- Best-corrected visual acuity (logMAR)

Imaging Protocol (2020 Guideline)

All patients:
SD-OCT + widefield FAF

VF testing (10-2 or 30-2):
Only when OCT or FAF abnormalities detected

mfERG:
When VF reliability was limited or structure–function correlation was unclear

Toxicity classified using revised RCOphth 2020 definitions

Comparator Cohort

Findings were compared with the Manchester audit performed under the 2018 RCOphth guideline, which reported:

- 566 at-risk patients screened
- Annual OCT, FAF and VF for all
- Definite toxicity in 1.06% (6/566)
- Possible toxicity in additional 0.7%

Differences in screening criteria, exposure duration and risk factor burden were considered in the comparative analysis.

RESULTS — Demographics

505

Total Patients Screened

87.5%

Female (442 / 505)

59 yrs

Mean Age

12.3 yrs

Mean HCQ Exposure

Daily Dosing Patterns

Dose	Patients (n)	Proportion
400 mg	291	57.6%
200 mg	174	34.5%
300 mg/day (standardised)	40	7.9%

Systemic Risk Factors

Risk Factor	n (%)
High dose relative to body weight	115 (22.8%)
Renal impairment	56 (11.1%)
Tamoxifen co-exposure	8 (1.6%)

Treatment Indications

Indication	n (%)
Rheumatoid arthritis	249 (50.7%)
Connective tissue diseases*	191 (37.8%)
Sjögren's spectrum disorders	33 (6.5%)
Autoimmune dermatological	15 (3.0%)
Other inflammatory/autoinflammatory†	14 (2.8%)

* SLE, mixed CTD, cutaneous/discoid lupus, dermatomyositis, scleroderma
† Sarcoidosis, antiphospholipid syndrome, Crohn's disease, autoimmune enthesitis

Visual Acuity (BCVA)

Well preserved in all patients:
Right eye: 0.14 logMAR (mean)
Left eye: 0.13 logMAR (mean)

Exposure Duration Detail

Mean HCQ exposure: 12.3 ± 7.4 years

This substantially exceeds the threshold at which toxicity risk rises markedly. The American Academy of Ophthalmology guidelines identify >5 years as the point where risk begins to increase significantly.

Patients in this cohort had a mean exposure over 12 years — a high-risk group by any metric.

Long exposure duration, combined with a 22.8% rate of high-dose therapy and 11.1% renal impairment, explains the higher prevalence of toxicity compared to earlier cohorts with shorter treatment histories.

RESULTS — Imaging & Toxicity

20

Definite HCQ Retinopathy (4.0%)

4

Possible Early Toxicity

17

Incidental OCT Pathology

12

Incidental FAF Pathology

Definite Retinopathy (n=20)

Characteristic parafoveal or pericentral outer retinal abnormalities on structural imaging.

All 20 cases identified through structural imaging (SD-OCT and/or widefield FAF) before visual field involvement.

This supports OCT as the most sensitive early marker of HCQ toxicity — abnormalities detectable structurally before functional loss occurs.

Four patients showed subtle but convincing OCT abnormalities while FAF and VF remained entirely normal.

Classified as possible early toxicity; under close follow-up with 3-monthly 10-2 visual field testing.

Demonstrates the precedence of structural over functional change in early HCQ toxicity.

Visual Field Testing — 41 Patients

VF performed only in cases with structural abnormalities (per 2020 guideline):

VF Outcome	n
Normal visual fields	21
Reproducible VF abnormalities	18
Unreliable — bipolar disorder (classified by imaging)	1
Unreliable — mfERG confirmed toxicity	1

Pathway Delays (n=8 patients)

- 2 patients — COVID-19 service disruptions
- 2 patients — No ophthalmic review for 15 and 27 years respectively
- 1 patient — Referral lost in transit
- 3 patients — VF appointment issues (misbooking, cancellation, deferred interpretation)

Despite low frequency, delays highlight gaps in cross-specialty coordination and the importance of consistent re-referral from GPs and Rheumatologists.

DISCUSSION

The definite toxicity prevalence of 4.0% (20/505) substantially exceeds rates reported in earlier UK studies conducted under the 2018 guideline.

In the Manchester cohort, definite toxicity was identified in 1.06% of at-risk patients (6/566), with an additional 0.7% showing possible toxicity.

Our combined definite-plus-possible prevalence of 4.8% is most plausibly explained by differences in cumulative exposure and risk burden:

- Longer mean HCQ exposure (12.3 vs 9 years)
- Higher rate of high-dose therapy (22.8%)
- Greater prevalence of renal impairment (11.1%)
- Tamoxifen co-exposure (1.6%)

The diagnostic criteria for definite and possible toxicity did not change between guidelines. What changed was the screening pathway — moving from routine annual VF for all to a structure-triggered approach.

Our findings show the 2020 pathway detected at least as many toxicity cases as VF-heavy protocols, validating the principle that SD-OCT is the most sensitive early marker of HCQ toxicity.

GUIDELINE COMPARISON

Feature	2018 Guideline	2020 Guideline
Baseline examination	Required	Removed
Annual SD-OCT	All patients	All patients
Annual widefield FAF	All patients	All patients
Annual visual field	All patients	Structural Δ only
mfERG	Not specified	Equivocal cases
Toxicity detected	~1.06%	4.0% (this cohort)

CONCLUSION

This retrospective evaluation of 505 patients screened 2021–2025 demonstrates that an imaging-led monitoring strategy as recommended in the 2020 RCOphth guideline is effective in detecting both early and definite HCQ retinopathy.

Higher toxicity prevalence compared with earlier cohorts reflects greater cumulative exposure and systemic risk burden rather than any change in diagnostic criteria.

Structural imaging also revealed incidental retinal pathology in a significant proportion of patients, underscoring the broader diagnostic value of SD-OCT and widefield FAF beyond HCQ toxicity screening.

The virtual clinic model is well suited to the updated guideline, enabling high-volume consistent imaging assessment without compromising diagnostic accuracy.

Enhanced awareness of monitoring responsibilities among HCQ-prescribing clinicians — particularly GPs and Rheumatologists — may facilitate earlier detection and reduce the risk of irreversible HCQ-related retinal damage.

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