

Hydroxychloroquine (HCQ) screening and Macular degeneration (AMD)

Improving pathways between Primary Care and HES

Ms Esther Posner
Medical Retina Unit, Western Eye Hospital

Hydroxychloroquine (HCQ) Screening in HES: the controversy!

Low risk and slow development toxicity – stopping drug may not prevent progression once early signs detected

So why was new guidance issued?

- 2009: RCOphth guidance: Screening not recommended
- 2018: new RCOphth Guidelines drawn up in collaboration with British Society for Rheumatology & British Association of Dermatologists.

– mainly based retrospective case-control study 2014 (Melles RB, Marmor MF¹) : retinopathy is ‘more common than previously reported’, with overall prevalence of 7.5%.

No reporting system - based on ad hoc audit data only.

Newer non-invasive imaging tests are now available in most eye units and thought pre-symptomatic changes can be picked up.

Not supporting a systematic screening programme was ‘no longer valid’.



LEVEL OF EVIDENCE USED

1. No RCTs or Grade A evidence exists to support a screening programme currently.

2. Reasonable level of evidence (Grade B) to support:

- HCQ > 5yrs annual screening
- Chloroquine (more toxic than HCQ) >1 yr – annual screening

3. Less evidence, designated as ‘Good Practice Points’ (GPP) – ie. not based on meta-analyses, systematic review, or extrapolated from studies with reasonable evidence weight to support:

- All those with any additional risk factors (above) annually from a baseline visit or annual before 5 yrs of treatment
- Responsibility of the prescribing physician (as per GMC guidelines) to refer eligible patients to the Hospital Eye Service (HES)
- Referring physician to complete a standardised referral proforma (attached) to determine risk and follow up period required.
- Organisation of services:
 - a. Take place in HES – virtual clinics: tests done by technicians and an ophthalmologist or AHP under supervision of consultant ophthalmologist then job-planned to interpret the images and decide on further management.
 - b. Written communication with screening outcome to patient, prescribing physician and GP
 - c. Failure to attend – not automatic discharge: requires a failsafe procedure
 - d. Work commitment for the ophthalmologist – sessional within job planning.

4. No evidence to support the following:

Baseline tests – recommended ideally within 6 months and definitely within 12 /12. Recommendation in the new guidelines to determine whether an individual can undergo screening and whether any other conditions of the eye exist which may make screening difficult or impossible.

The Royal College of Ophthalmologists issued the following statement in June 2018 as a result of widespread confusion over the funding for this new service:

“Ophthalmologists are not the prescribers therefore it is not the responsibility of ophthalmologists to resource the screening. The responsibility belongs to the dermatologists and rheumatologists.”

Currently, there has been no funding agreed to set up the infrastructure required to screen these patients according to the new guidelines.

Until such funding is secured, the Ophthalmology department at Imperial College Healthcare NHS Trust is unable to see patients for screening as per the new guidelines but will continue to accept the following patients as previously:

1. Duration of use >5 yrs
2. New visual symptoms in patients on HCQ

Risk factors to note in referrals:

1. Dose – 5mg/kg maximal
2. Low risk for first 5 years:

Melles and Marmor: daily consumption 4.0 to 5.0 mg/kg, prevalence of retinal toxicity remained < 2% within the first 10 years of use but almost 20% after 20 years of use.

Overall prevalence quoted at 7.5%.

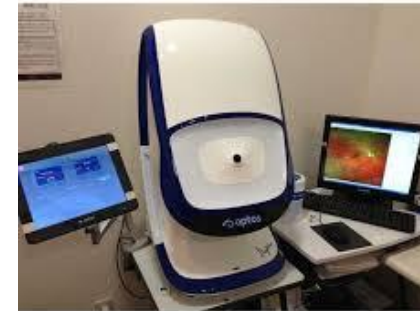
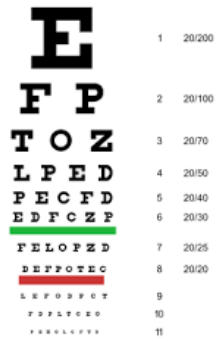
3. Concomitant tamoxifen therapy.
4. Renal insufficiency (eGFR <50 ml/min/1.73m²)
5. Chloroquine (cf. Hydroxychloroquine) rarer use but more toxic – annual screen if >2.3mg/kg

15. Referral form for specialists/general practitioners to complete when referring to the ophthalmology service for hydroxychloroquine screening

<p>Date:</p> <p><u>Referring Consultant Clinician</u></p> <p>Name:</p> <p>Contact email:</p> <p>Specialty (<i>please circle</i>): Rheumatology / Dermatology</p>	<p><u>Patient Details (sticker)</u></p> <p>Name:</p> <p>D.O.B:</p> <p>NHS:</p>
<p><u>Essential Information</u></p> <ul style="list-style-type: none"> ▪ Date hydroxychloroquine (or chloroquine) commenced:/...../..... OR Total Duration of treatment if non-continuous: ____/____ (<i>years/months</i>) ▪ Daily Dose: _____mg ▪ Body weight: _____kg ▪ Tamoxifen use (past or present): Yes/No (<i>please circle</i>) ▪ Renal Function (please give most recent): GFR _____ Date recorded:/...../..... ▪ Other medication (<i>please list all</i>) ▪ Any known eye condition: Yes/No <ul style="list-style-type: none"> ▪ If Yes please give details 	<p><u>GP Details</u></p> <p>Name:</p> <p>Address:</p> <p>Postcode:</p>

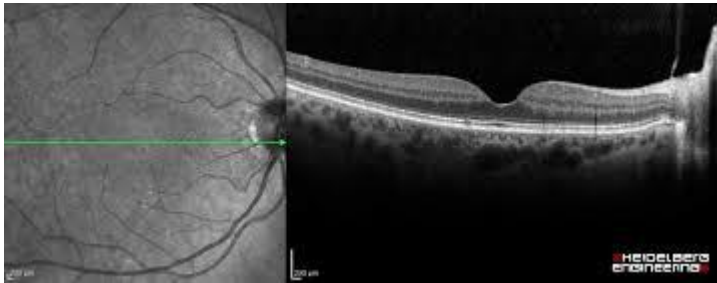
Economic implications for delivery of the new guidance

Tests required per appointment (per eye) 45-50 mins :

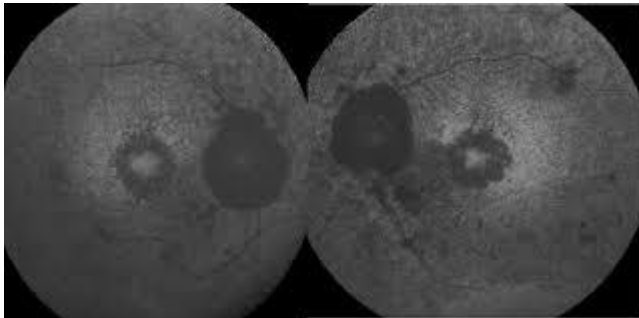


Interpretation of tests and written report (per eye):

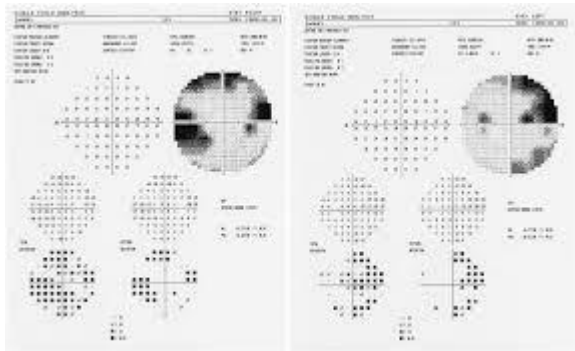
1.



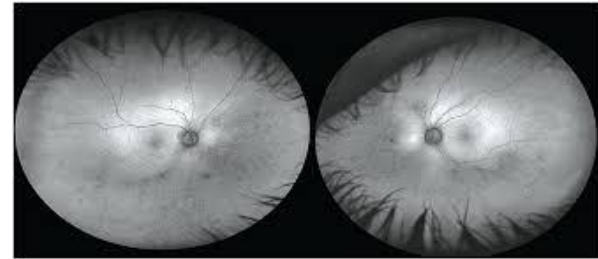
2.



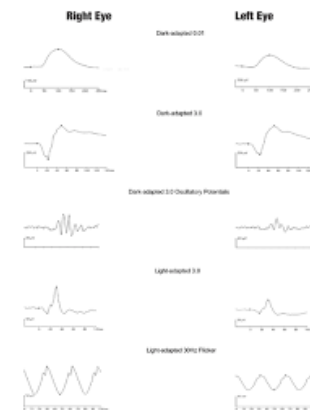
3.



4.



5.



Staffing infrastructure

1. Numbers of anticipated new referrals is high (3-4 000 at Imperial) – requires at least 1 new weekly clinic for diagnostics – nurse + technician - then follow up as virtual review by a consultant
2. Administration – requires a Failsafe officer
3. Major capacity issues exist already in HES across UK – particularly MR and glaucoma units managing high risk blinding conditions.

Why has this not gone through national screening committee which would then be funded nationally?

To determine cost -effectiveness, need epidemiological data + relevant measure of beneficial effect of screening (sight preservation) identified.

College states that unless its recommendations for screening are instituted, not possible to calculate cost effectiveness.

Accepts: no study that has compared screening methods.

Also accepts: lack of grade A evidence.

IE. currently insufficient data to fulfil UK National Screening Committee consideration.

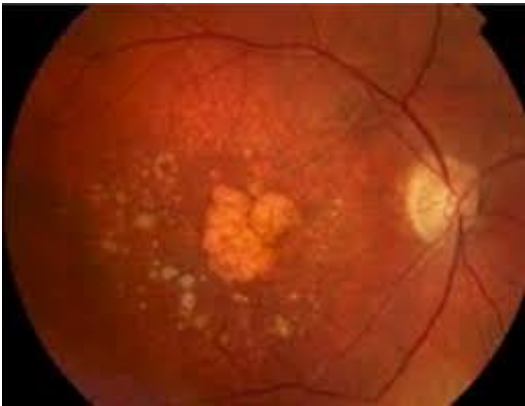
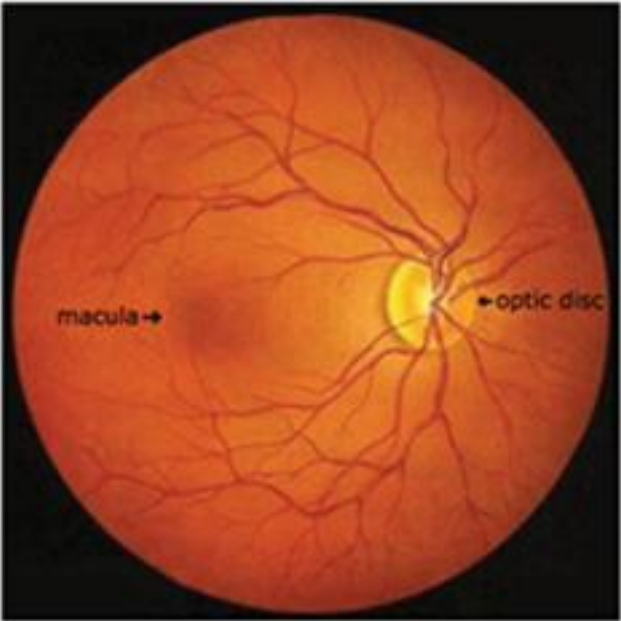
<https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme>



Age-related Macular Degeneration (AMD)

Common abbreviations in the eye clinic letters

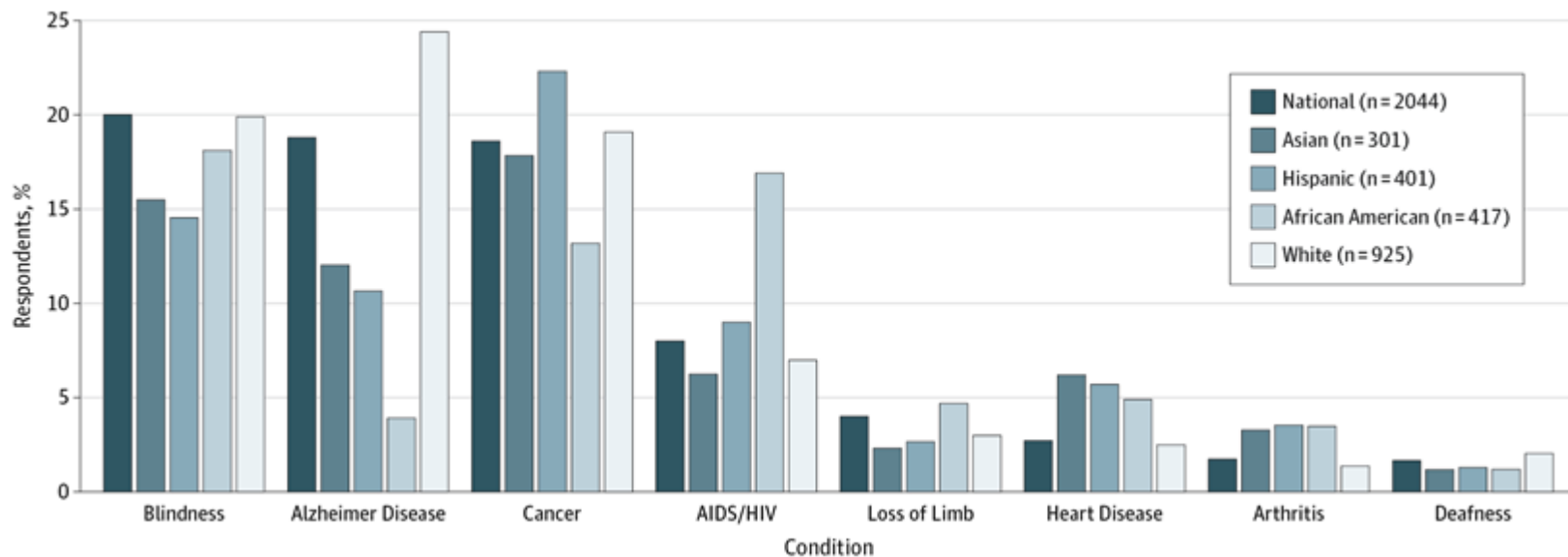
- wAMD/cnvm – wet AMD/choroidal neovascular membrane – antiVEGF injections
- Dry AMD/geographic atrophy (GA) – much more common – no treatment currently
- LVA – Low Vision Assessment
- CVI – certificate visual impairment (SI – sight-impaired, SSI – severe sight-impaired)
- IVT – intravitreal therapy (injections)
- AntiVEGF (vascular endothelial growth factor) – Lucentis, Eylea, Avastin
- AREDS2 – Age-Related Eye Disease Study, multivitamin study
- Macula – central part of the retina, responsible for visual acuity
- VF – visual fields (24-2, 10-2 describes degrees of field being tested)
- OCT – optical coherence tomography (OCT-A: OCT angiography)
- FAF – fundus autofluorescence
- UWF – ultra-widefield imaging
- FFA – fundus fluorescein angiography
- EDT – electrodiagnostic testing – highly specialised, few units (MEH, WEH)

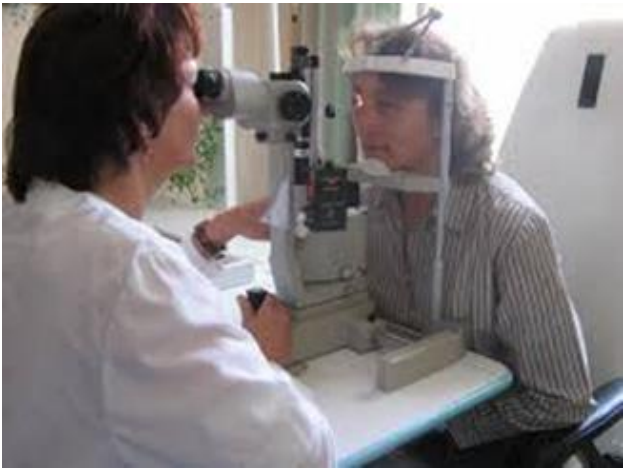


Public Attitudes About Eye and Vision Health

Adrienne W. Scott, MD1; Neil M. Bressler, MD1,2; Suzanne Ffolkes, BA, MA3; et al John S. Wittenborn, BS4; James Jorkasky, MBA5
JAMA Ophthalmol. 2016;134(10):1111-1118.

Rankings of Worst Conditions









Multivitamin supplementation – AREDS2 study

2001: NIH National Eye Institute: Age-Related Eye Disease Study (AREDS) - nutritional supplement called the AREDS formulation can reduce risk of developing advanced age-related macular degeneration (AMD). The original AREDS formulation contains vitamin C, vitamin E, beta-carotene, zinc and copper.

-  Vision loss by 19%
-  Risk of advanced AMD by 25%

Not a cure for AMD, nor reversal of visual loss.

Not preventative in early cases with no visual loss.

But have role reducing patients at high risk from developing advanced AMD.

Multivitamin supplementation – AREDS2 study

2006: same research group ran AREDS2

Added omega-3 fatty acids + the antioxidants lutein and zeaxanthin (in same family of nutrients as beta-carotene) as prior studies had associated beta-carotene with ↑ risk lung cancer in smokers.

Result:

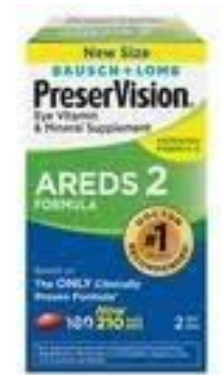
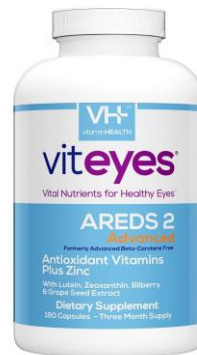
- omega-3 fatty acids had no effect
- lutein and zeaxanthin together safe + effective alternative to beta-carotene.

Examples:

PreserVision

VitEyes

Macushield Gold



Thank you

Questions/Comments ?

e.posner@nhs.net