Study Questions	Information	Recommendations
Diabetes Mellitus		
WESDR: WISCONSIN EPIDEMIOLOGIC STUDY OF DIABETIC RETINOPATHY		
Epidemiological study of diabetic retinopathy		i) Duration of diabetes is directly associated with increased prevalence of diabetic retinopathy. ii) Type I: Onset of DM < 30 years. iii) Type II: Onset of DM > 30 years.
UKPDS: UNITED KINGDOM PROSPECTIVE DIABETES STUDY		
Q: Will intensive control of **blood glucose**, in patients with **diabetes mellitus type 2** reduce the risk of microvascular complications of diabetes including the risk of retinopathy progression? Q: Will intensive control of **blood glucose**, in patients with **diabetes mellitus type 2** and elevated blood pressure reduce the risk of microvascular complications of diabetes including the risk of retinopathy progression?	Drugs used: OHA and insulin ACE inhibitors and beta blockers	R1: Intensive control of blood glucose reduced: i) risk of retinopathy progression ii) risk of microvascular complications of diabetes R2: Intensive control of blood pressure reduced: i) risk of retinopathy progression ii) risk of microvascular complications of diabetes.
DCCT: DIABETES CONTROL AND COMPLICATIONS TRIAL		
Q: Will intensive control of blood glucose slow development and subsequent progression of diabetic retinopathy in **diabetes mellitus type 1**?	Group1: No DR Group 2: Mild to moderate DR	Intensive control of blood glucose reduced the risk of i) developing DR by 76% ii) slowed progression of DR by 54% iii) developing neuropathy by 60% iv) developing albuminuria by 54%

ETDRS: EARLY TREATMENT OF DIABETIC RETINOPATHY		
Q: Is photocoagulation effective for treating diabetic macular oedema? Q: Is photocoagulation effective in treating diabetic retinopathy? Q: Is aspirin effective for preventing progression of diabetic retinopathy?	3711 patients Mild NPDR to Early PDR. Scatter or focal laser Aspirin 650mg/d	R1: Focal photocoagulation in diabetic macular oedema i) reduced retinal thickening. ii) reduced the risk of moderate vision loss (MVL) i.e. doubling of visual angle. iii) increased the chance of moderate visual gain i.e. halving the visual angle. R2: Early scatter photocoagulation is i) not indicated in mild to moderate NPDR ii) resulted in small reduction in the risk of sever vision loss (SVL) iii) is most effective in type 2 diabetes. R3: Aspirin reduced cardiovascular morbidity and mortality.
DRS: DIABETIC RETINOPATHY STUDY		
Q: Is panretinal photocoagulation (Argon of Xenon arc) effective for treatment of diabetic retinopathy?	1742 patients Bilateral severe NPDR Or PDR	R1: PRP resulted in 50% or greater reduction in the risk of SVL in treated eyes than control eyes over 5 years. R2: Treated eyes with high risk PDR achieved greatest benefit.
DRVS: DIABETIC RETINOPATHY VITRECTOMY STUDY		
Q: Is early vitrectomy (1-6 months after onset of vitreous haemorrhage) preferable to deferral of vitrectomy (at 1 year) in eyes with severe vitreous haemorrhage with PDR or very severe PDR?		R1: Visual acuity 20/40 or better was more frequent in early vitrectomy groups. R2: Benefit of early vitrectomy was seen only in eye with most severe PDR.

Age Related Macular Degeneration		
AREDS: AGE RELATED EYE DISEASE STUDY		
Q: Evaluate incidence of age related cataract and age related macular degeneration. Q: Evaluate the associated risk factors. Q: Evaluate whether antioxidants or zinc supplements can reduce development or progression of cataract or AMD.	4757 subjects Age group: 55-80 years	R1:High risk group for AMD progression or vision loss due to AMD: i) extensive intermediate drusen ii) at least one large druse iii) noncentral geographic atrophy iv) advanced AMD in one eye R2: Consider supplementation for these patients with: i) Vitamin C: 500mg ii) Vitamin E: 400 IU iii) Beta carotene: 15mg iv) Zinc oxide: 80 mg v) Cupric oxide: 2mg R3: Avoid smoking, maintain balanced diet R4: No role of lutein in prevention of AMD
PTAMD: PROPHYLACTIC TREATMENT OF AMD TRIAL		
Q: To determine the effect of 810nm diode laser on development of neovascular AMD and visual acuity in eyes with multiple large drusen with fellow eye having neovascular AMD.	48 spot grid laser treatment	R1: Treated eyes had higher incidence of i) vision loss ii) development of neovascular AMD
MPS: MACULAR PHOTOCOAGULATION STUDY		
Argon Study: Whether argon blue-green laser photocoagulation of extrafoveal CNVM (200-2,500 microns from the centre of FAZ) is of benefit in preventing vision loss in AMD, presumed ocular Histoplasmosis (POH), and idiopathic neovascular membranes (INVM).		R1: For patients with any of the three above conditions, eyes with well-demarcated areas of classic CNVM, as defined by fluorescein angiography, had a better visual prognosis when treated with laser photocoagulation, performed according to MPS guidelines,

Krypton Study: Whether krypton red laser photocoagulation of juxtafoveal CNVM (1-199 microns from the centre of the FAZ) is of benefit in preventing vision loss in patients with AMD, POH, and INVM. **Foveal Study**: Whether laser photocoagulation is of benefit in preventing vision loss in patients with subfoveal CNVM.		than when managed by observation. These outcome data apply to all three conditions when the position of the neovascularization is extrafoveal or juxtafoveal. R2: Eyes with AMD and subfoveal CNVM benefited more from laser treatment than from observation when MPS eligibility guidelines and treatment protocol were observed. Overall, eyes receiving direct laser treatment to the fovea for new CNV immediately lost more visual acuity than observed eyes. However, the amount of visual acuity loss in observed eyes increased to the level of loss in treated eyes at 12 months and exceeded the level thereafter. Eyes with smaller lesions and worse initial visual acuity had greater and earlier benefits of laser treatment.
TAP: TREATMENT OF AGE RELATED MACULAR DEGENERATION WITH PHOTODYNAMIC THERAPY		
Q: If photodynamic therapy with Verteporfin reduces the risk of vision loss in subfoveal CNVM?	New or recurrent CNV Classic component size $\leq$ 5400 microns Blood < 50% Vision:20/40 -20/200	R1: In treated group, 59% of subjects lost less than 15 letters in comparison to 31% in placebo group when the lesion was **predominantly classic**.

VIP: VERTEPORFIN IN PHOTODYNAMIC THERAPY		
Q: If photodynamic therapy with Verteporfin reduces the risk of vision loss in subfoveal CNVM due to AMD and pathological myopia?	New or recurrent CNV Total CNV area $\leq$ 5400 microns **Occult CNV** Recent disease progression	R1: In treated group, 49%% of subjects had SVL in comparison to 75% in placebo group when the lesion was **smaller than 4 disc diameter and baseline visual acuity was less than 20/50.**
MARINA: MINMALLY CLASSIC/OCCULT TRIAL OF ANTI VEGF ANTIBODY RANIBIZUMAB IN NEOVASCULAR AMD		
Q: Whether monthly intravitreal injections of Ranibizumab prevented vision loss from neovascular AMD?	0.3mg and 0.5mg monthly	R1: Among treated group 95% subjects lost less than 15 lines on standard visual acuity chart than 62% in placebo group. R2: Among treated group 34% subjects gained 15 lines or more on standard visual acuity chart.
ANCHOR: ANTI-VEGF ANTIBODY FOR THE TREATMENT OF PREDOMINANTLY CLASSIC CNV IN AMD		
Q: To compare Ranibizumab versus Verteporfin in the treatment of neovascular AMD.	0.5mg intravitreal injection	R1: Among Ranibizumab group 96% subjects lost less than 15 lines on standard visual acuity chart than 64% in Verteporfin group. R2: Among Ranibizumab group 40% subjects gained 15 letters or more on standard visual acuity chart than 6% in Verteporfin group.

PIER: PHASE IIIb SHAM INJECTION CONTROLLED STUDY OF THE SAFETY AND EFFICAY OF RANIBIZUMAB		
Q: To assess whether fewer injections of Ranibizumab can result in better visual outcomes than sham-injected controls?	3 monthly injection of Ranibizumab	R1: Subjects receiving 3 monthly injection of Ranibizumab initially gained vision for 3 months then returned to baseline at 12 months. Sham injection subjects lost continuously over the follow up.
SANA: SYSTEMIC AVASTIN FOR NEOVASCULAR AMD		
Q: Whether systemic Avastin in neovascular AMD results in improvement in visual acuity?	5mg/kg every 2 weeks for 2-3 months	R1: At 12 weeks Avastin group had significant improvement in mean visual acuity and central retinal thickness.
Other Studies in Retina & Vitreous		
CVOS: CENTRAL VEIN OCCLUSION STUDY GROUP		
Q: Whether photocoagulation therapy can help prevent iris neovascularization in eyes with central vein occlusion (CVO) and evidence of ischemic retina. Q: Whether grid-pattern photocoagulation therapy will reduce loss of central visual acuity due to macular oedema secondary to CVO.	Green argon laser	R1: Macular grid photocoagulation was effective in reducing angiographic evidence of macular oedema but did not improve visual acuity in eyes with reduced vision due to macular oedema from CVO. R2: Prophylactic panretinal photocoagulation did not prevent the development of iris neovascularization in eyes with 10 or more disc areas of retinal capillary nonperfusion confirmed by fluorescein angiography. Rather, results of this randomized clinical trial demonstrate that it is safe to wait for the development of early iris neovascularization and then apply panretinal photocoagulation. R3: Eyes with such extensive intraretinal

		haemorrhage that it is not possible to determine the retinal capillary perfusion status act as if they are ischemic or nonperfused.
BVOS: BRANCH VEIN OCCLUSION STUDY GROUP		
Q1: Whether scatter laser photocoagulation can prevent the development of neovascularization? Q2: Whether peripheral scatter laser photocoagulation can prevent vitreous haemorrhage? Q3: Whether macular laser photocoagulation can improve visual acuity in eyes with macular oedema reducing vision to 20/40 or worse.	Green argon laser	R1: Macular argon laser photocoagulation improves vision in BRVO macular oedema. R2: Scatter argon laser photocoagulation reduces the risk of development of neovascularization in eyes with BRVO involving an area of 5 disc diameters. R3: Scatter argon laser photocoagulation reduces the risk of vitreous haemorrhage in eyes with BRVO with neovascularization.
ONTT: OPTIC NEURITIS TREATMENT TRIAL		
Q1: To assess the beneficial and adverse effects of corticosteroid treatment for optic neuritis. Q2: To determine the natural history of vision in patients who suffer optic neuritis. Q3: To identify risk factors for the development of multiple sclerosis in patients with optic neuritis.	Oral prednisone (1 mg/kg/day) for 14 days. Intravenous methylprednisolone (250 mg every 6 hours) for 3 days. Oral prednisone (1 mg/kg/day)	R1: Brain MRI is a powerful predictor of the early risk of multiple sclerosis after optic neuritis. R2: Low 5-year risk of multiple sclerosis (cases without MRI lesions): i) lack of pain ii) optic disc oedema iii) peripapillary haemorrhage iv) retinal exudates v) mild visual loss R3: Visual recovery begins rapidly (within 2 weeks) in most patients without any treatment, and then improvement

	for 11 days. Oral placebo for 14 days	continues for up to 1 year. Most patients recover to 20/20 or near 20/20 acuity. R4: The probability of a recurrence of optic neuritis in either eye within 5 years is 28 percent. R5: Intravenous methylprednisolone followed by oral corticosteroid: i) accelerated visual recovery ii) no long-term benefit to vision iii) short-term reduction in the rate of development of multiple sclerosis R6: Oral prednisone: i) no improvement in visual outcome ii) increased rate of new attacks of optic neuritis
EVS: ENDOPHTHALMITIS VITRECTOMY STUDY		
Q1: To determine the role of initial pars plana vitrectomy in the management of postoperative bacterial endophthalmitis. Q2: To determine the role of intravenous antibiotics in the management of bacterial endophthalmitis. Q3: To determine factors which predict outcome in postoperative bacterial endophthalmitis?		R1: Immediate vitrectomy tripled the rate of achieving 20/40 final visual acuity in subjects presenting with light perception vision. R2: In patients presenting with hand movement or better visual acuity; there was no difference in final visual outcome with or without immediate vitrectomy. R3: There was no difference in final visual acuity or media clarity with or without systemic antibiotics.

SILICON STUDY		
Q: To compare the postoperative tamponade effectiveness of intraocular silicone oil with that of an intraocular long-acting gas (initially sulphur hexafluoride [SF6], later perfluoropropane [C3F8]) for the management of retinal detachment complicated by proliferative vitreoretinopathy (PVR).		R1: Silicon oil tamponade resulted in better visual acuity than SF6. R2: Silicon oil more frequently resulted in macular attachment than SF6. R3: There was no difference in final visual acuity or posterior retinal reattachment with silicon oil or C3F8 tamponade. R4: Silicon oil and C3F8 produced better results than SF6.
Glaucoma		
MOORFIELDS PRIMARY TREATMENT TRIAL		
Q: Newly diagnosed POAG: medicine vs. laser trabeculoplasty vs. trabeculectomy		R1: Lowering of IOP and preservation of vision was highest with trabeculectomy.
GLAUCOMA LASER TRAIL		
Q: Newly diagnosed POAG: medicine vs. laser trabeculoplasty.		R1: Initial laser trabeculoplasty is as effective as initial timolol maleate to reduce IOP and preserve vision.
FLUOROURACIL FILTRATION SURGERY TRIAL		
Q: Whether post-operative subconjunctival 5 fluorouracil increases success rate in patients with risk of failure after glaucoma filtration surgery?		R1: Subconjunctival 5FU results in better control of IOP in high risk cases. R2: Visual acuity at follow up remains the same in both groups.

CNTGS: COLLABORATIVE NORMAL TENSION GLAUCOMA STUDY		
Q: Whether lowering of IOP by 30% reduces the risk of progression of glaucomatous damage in normal tension glaucoma eyes?		R1: Lowering of IOP by medical/laser/trab reduces the progression of disease from 35% (untreated) to 12% (treated).
AGIS: ADVANCED GLAUCOMA INTERVENTION STUDY		
Q: Comparison of various treatment modalities for advanced glaucoma with failure of medical therapy.		R1: Black patients: better results with argon laser trabeculoplasty first. R2: White patients: better result with trabeculectomy first. R3: Male subjects are at greater risk of bleb encapsulation. R3: Low IOP has protective role in visual field deterioration. R4: ALT failure: younger age, high pre-intervention IOP R5: Trabeculectomy failure: younger age, high pre-intervention IOP, diabetes mellitus Post-operative increased IOP and inflammation.

CIGTS: COLLABORATIVE INITIAL GLAUCOMA TREATMENT STUDY		
Q: Newly diagnosed POAG: medicine vs. filtration surgery		R1: Filtration surgery resulted in better IOP control. R2: Visual acuity and visual filed loss was more in surgery group for first 3 years with higher visual symptoms and cataract formation.
OHTS: OCULAR HYPERTENSION TREATMENT STUDY		
Q: Ocular hypertensive patients: medicine vs. observation.		R1: IOP reduction reduced the risk of visual field progression from 9.5% to 4.4%. R2: Treatment is recommended for ocular hypertensives with moderate to severe risk of developing POAG. R3: Family history of glaucoma, MD, CPSD, myopia, migraine, CVA, hypertension, hypotension, beta blockers, calcium channel blockers are NOT associated with risk of developing POAG. R4: Diabetes mellitus has a protective role against development of POAG in ocular hypertension.
EMGT: EARLY MANIFEST GLAUCOMA TRIAL		
Q: Newly diagnosed POAG: Immediate treatment (betoxolol/ALT) vs. late or no intervention.		R1: A 25% reduction in IOP reduces the risk of progression of POAG from 49% to 30% with observation alone.

Cornea		
HEDS I: HERPETIC EYE DISEASE STUDY I		
Q: **Topical corticosteroids** in herpes simplex stromal keratitis in conjunction with topical trifluridine. Q: **Oral acyclovir** in herpes simplex stromal keratitis in conjugation with topical corticosteroids and trifluridine. Q: **Oral acyclovir** in herpes simplex iridocyclitis in conjunction with topical corticosteroids and trifluridine.		R1: Topical corticosteroids resulted in faster resolution of stromal keratitis. R2: No apparent benefit in the addition of oral acyclovir to the treatment regimen of a topical corticosteroid and a topical antiviral. R3: Benefit in adding oral acyclovir to the treatment in patients receiving topical corticosteroids and trifluridine prophylaxis.
HEDS II: HERPETIC EYE DISEASE STUDY II		
Q: Whether early treatment with **oral acyclovir** of herpes simplex epithelial keratitis prevents progression to stromal keratitis and iridocyclitis. Q: Whether **low-dose oral acyclovir** is effective in preventing recurrent HSV eye infection in patients with previous episodes of herpetic eye disease. Q: Whether **external factors** (ultraviolet light or corneal trauma) and behavioural factors (life stress) on the induction of ocular recurrences of HSV eye infections and disease.		R1: No benefit from the addition of oral acyclovir to treatment with topical trifluridine in preventing the development of stromal keratitis or iritis. R2: Oral acyclovir reduced the incidence of recurrent herpes disease by 41 percent. R3: No proved result was found.

Miscellaneous		
COMS: COLLABORATIVE OCULAR MELANOMA STUDY		
Q1: To compare the effectiveness of brachytherapy to enucleation for treatment of medium-size choroidal melanomas. Q2: To assess the effectiveness of enucleation with and without preoperative external-beam radiotherapy for large choroidal melanomas.		R1: No difference in the 5 year survival with either brachytherapy or enucleation. R2: Preoperative radiation for large choroidal melanomas does not improve 5 year survival rate.
ETROP: EARLY TREATMENT OF RETINOPATHY OF PREMATURITY		
Q: Whether earlier treatment in carefully selected cases will result in an overall better visual outcome?		R1: Retinal ablation is indicated in: i) zone I ROP: any stage with plus disease. ii) zone I ROP: stage 3, no plus disease. iii) zone II ROP: stage 2 or 3 with plus disease.