



MASSACHUSETTS  
EYE AND EAR



HARVARD MEDICAL SCHOOL  
TEACHING HOSPITAL

# *How we should be treating angle closure in the modern era*

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**I have no disclosures  
relevant to this talk**

# Glaucoma Worldwide

- Affected\*

	POAG	PACG
2014	44 million	21 million
2020	63 million	30 million

## Blind from Glaucoma\*\*

2010	4.5 million	3.9 million
2020	5.9 million	<b>5.3 million</b>

Tham, 2013\*, Quigley 2006\*\*

# PACG 40 – 80 years of age

*Region*

*Prevalence (%)*

**Asia**

**1.1**

**North America**

**Latin America and Caribbean**

**Africa**

**Oceania**

**Europe**

**0.25 – 0.8**

Tham, Ophthalmology, 2013

# PACG 40 – 80 years of age

*Region*

*Population  
(millions)*

**Africa**

**1.3**

**North America**

**Latin America and Caribbean**

**2.0**

Asia

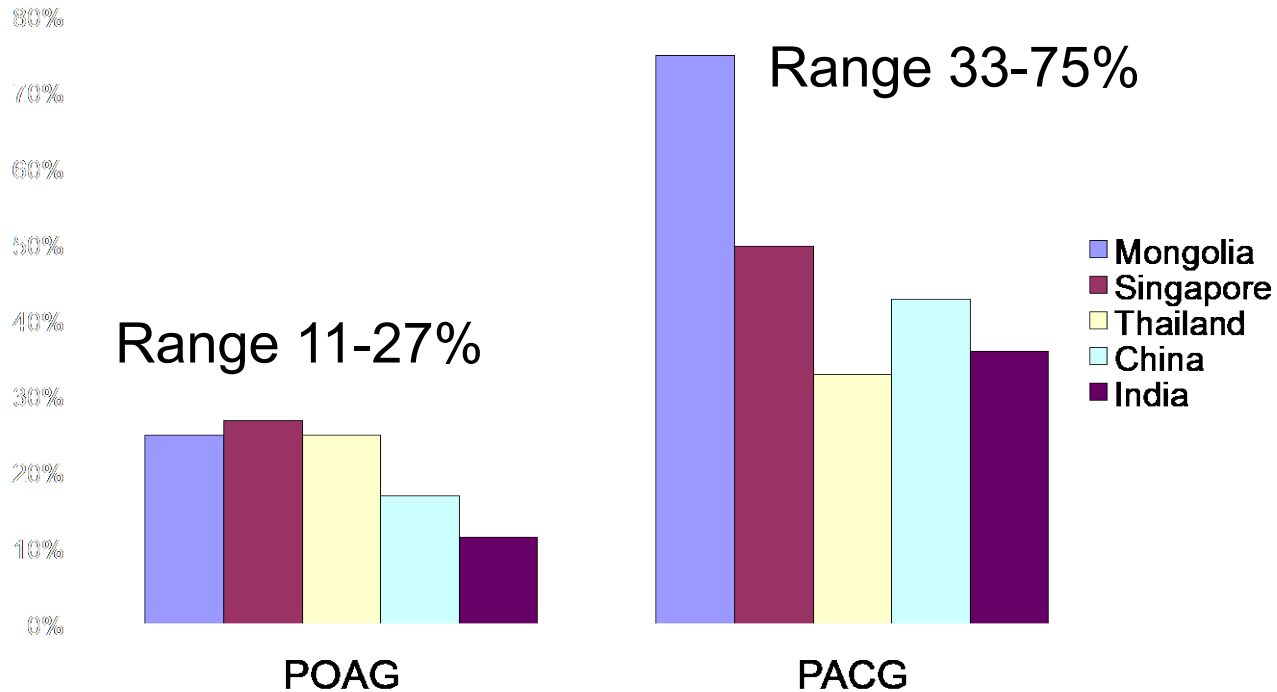
Oceania

Europe

**17**

Tham, Ophthalmology, 2013

# Blindness rates: PACG > POAG

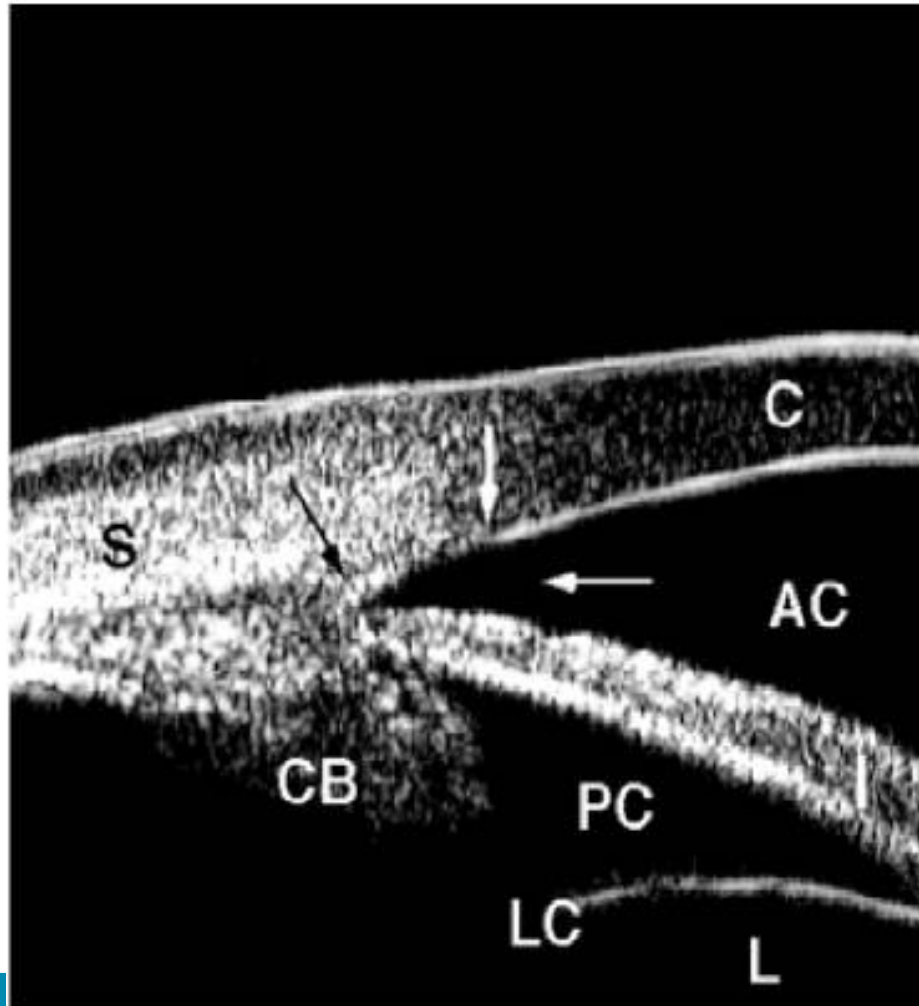


Proportion of unilateral blindness in population surveys

# Summary of angle closure rates (over 40)

Chinese	0.5 – 1.5%
Indians	0.5% - 1%
Japan	0.5%
Korea	0.7%
Thailand	0.9%
<b>Myanmar</b>	<b>2.3%</b>
African-derived	0.6%
European-derived	0.3 - 0.6%

# UBM





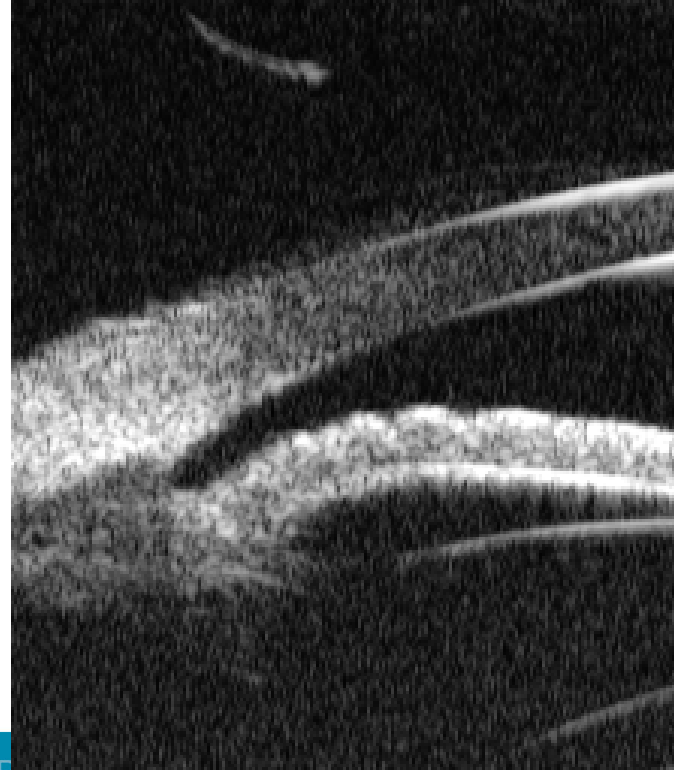
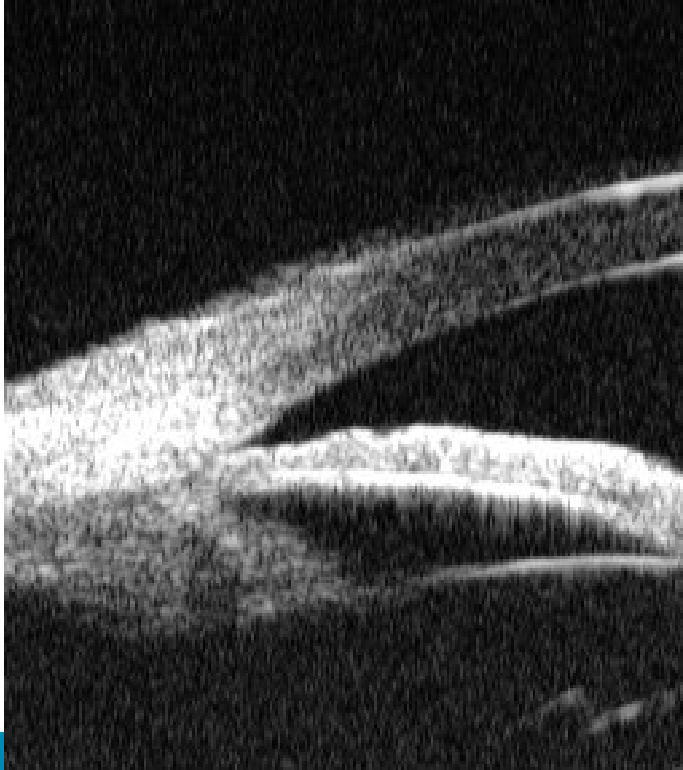
# Open Versus Closed Angles



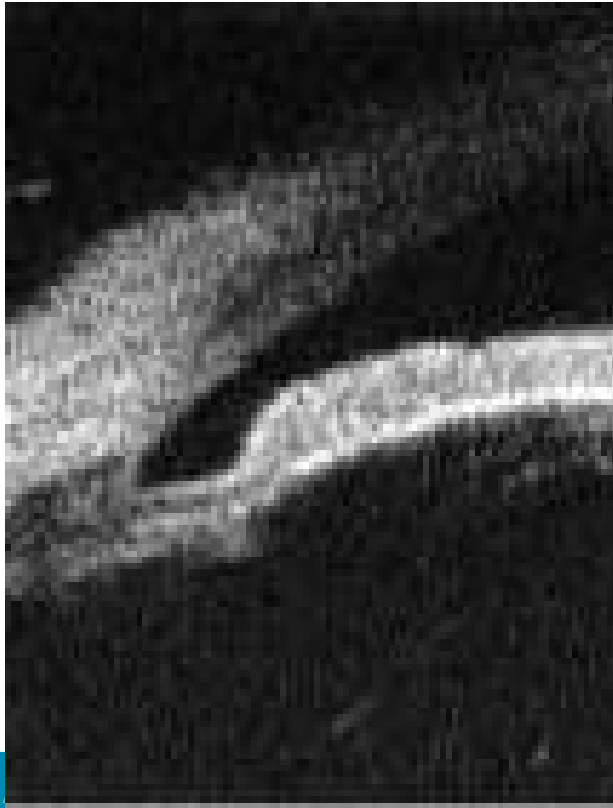
# Iris Thickness



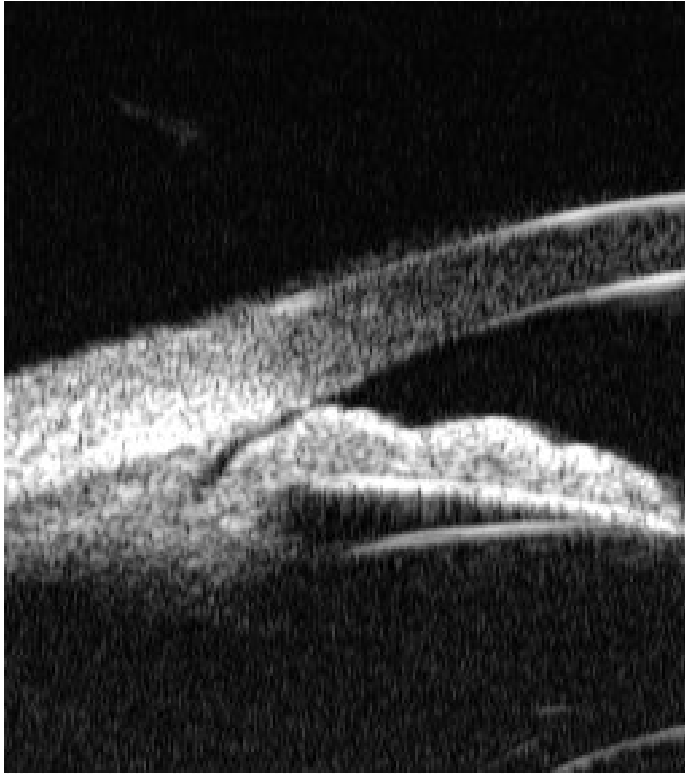
# Iris Insertion



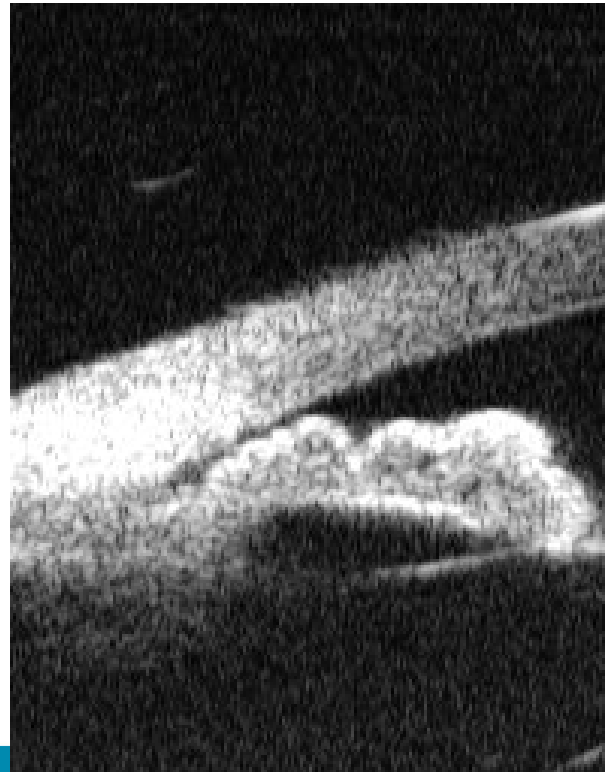
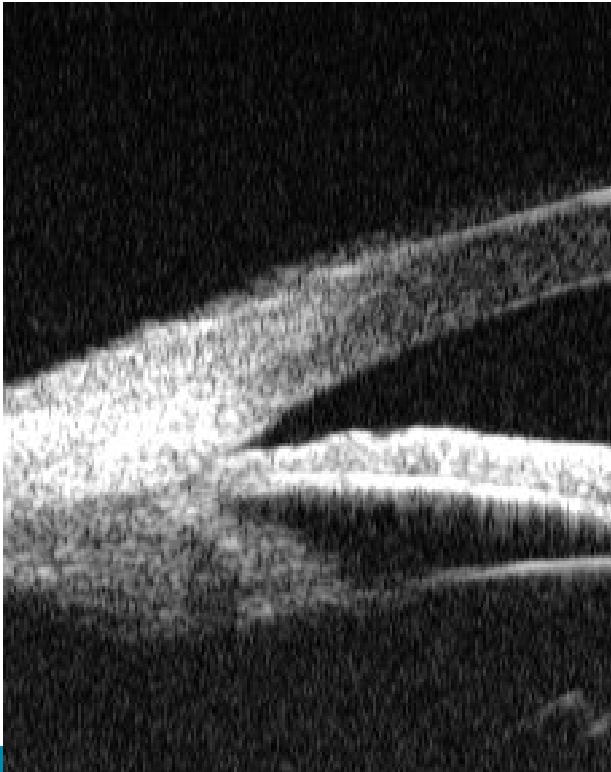
# Iris Insertion



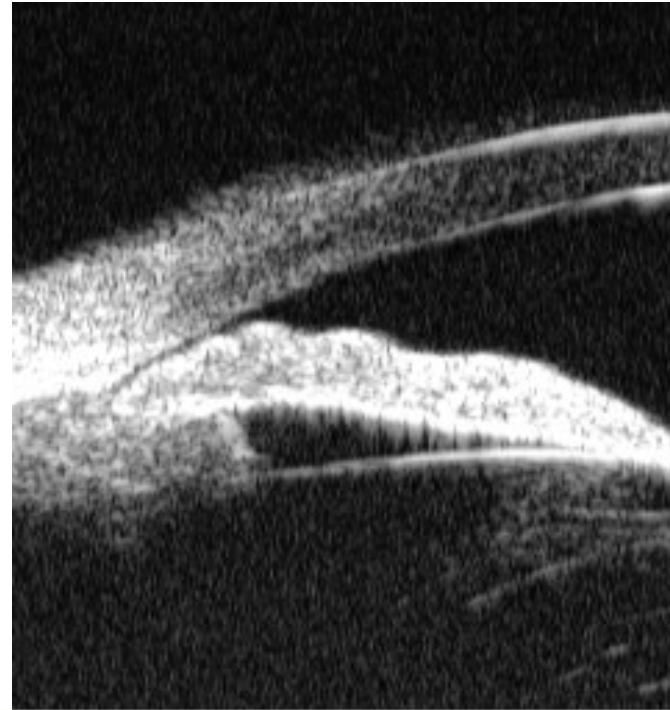
# Iris Configuration



# “Iris Roll”



# Plateau Configuration



# Angle Closure Terminology



# Primary Angle Closure Suspect

No evidence of disease

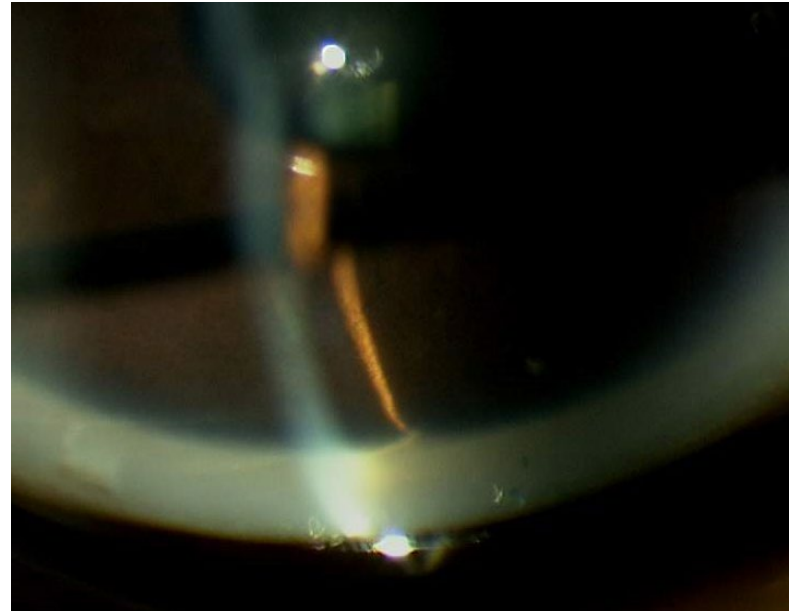
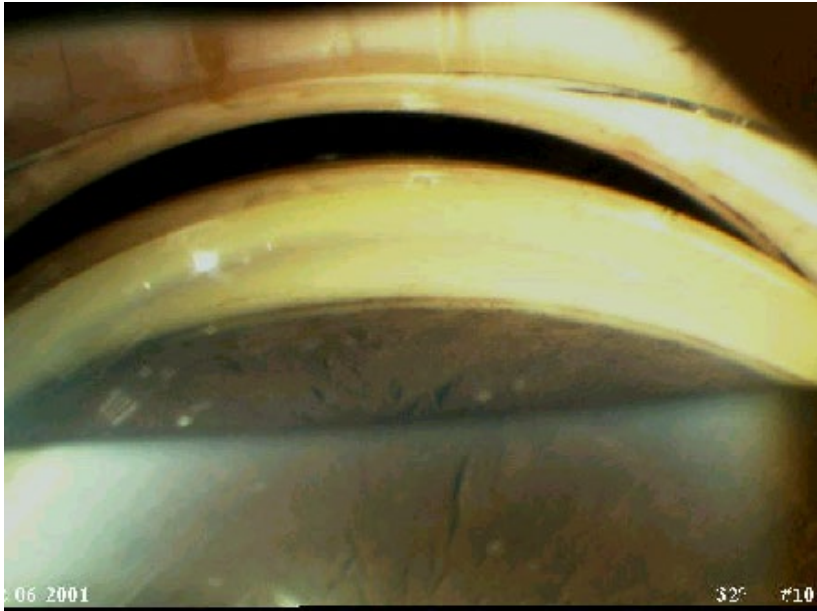
No visible posterior TM

270 degrees ( or 180 degrees)

IOP < 95 percentile for the population

**No disc or field damage**

# Primary Angle Closure Suspects



# Primary Angle Closure

Iridotrabecular contact

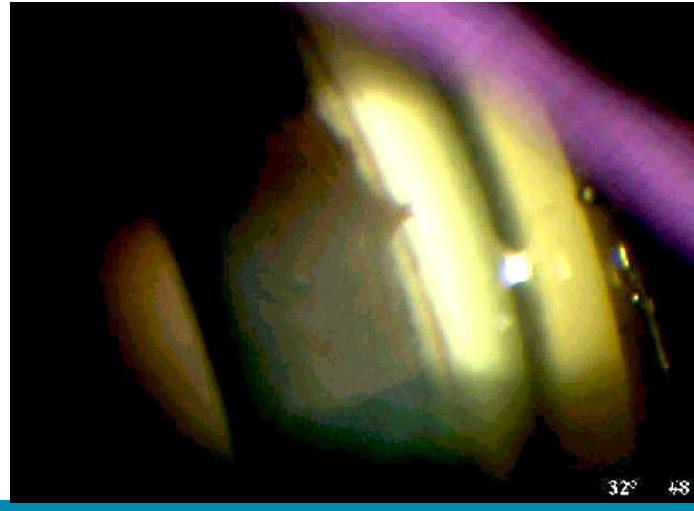
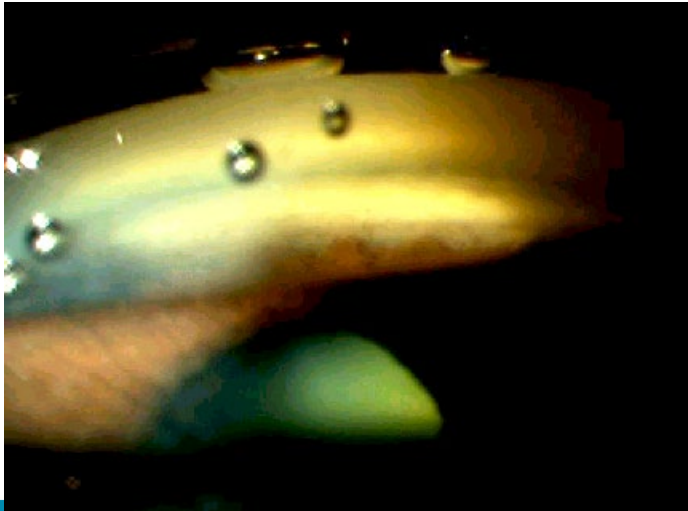
**Evidence of secondary effect**

No disc or field damage

# Primary Angle Closure

Peripheral anterior synechiae

Elevated IOP



# “Iridotrabecular Contact” and IOP

Elevated IOP with narrow angles unlikely due to chance

If narrow angles = 20%, elevated IOP = 5%

**Both at the same time is 1%**



# Acute angle closure crisis

Sudden elevation in eye pressure associated with a closed angle

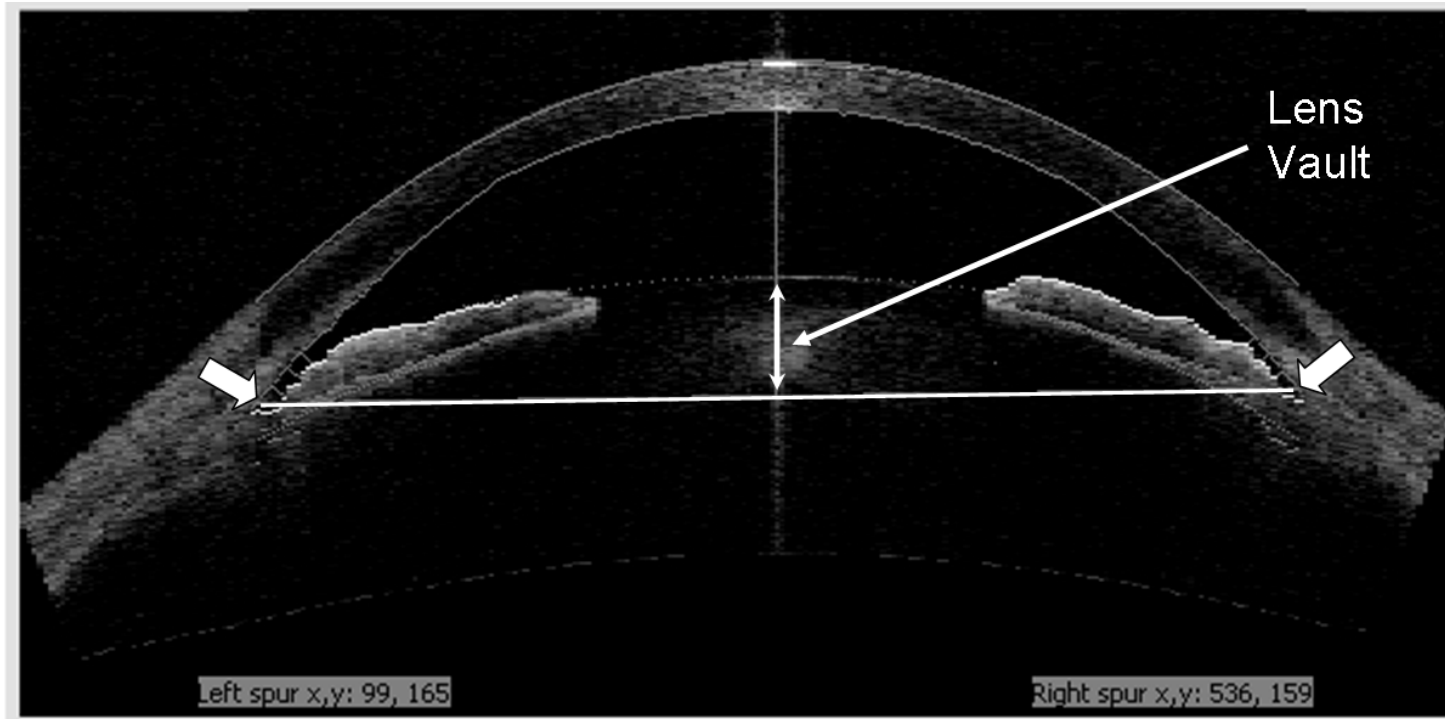
Classic signs and symptoms



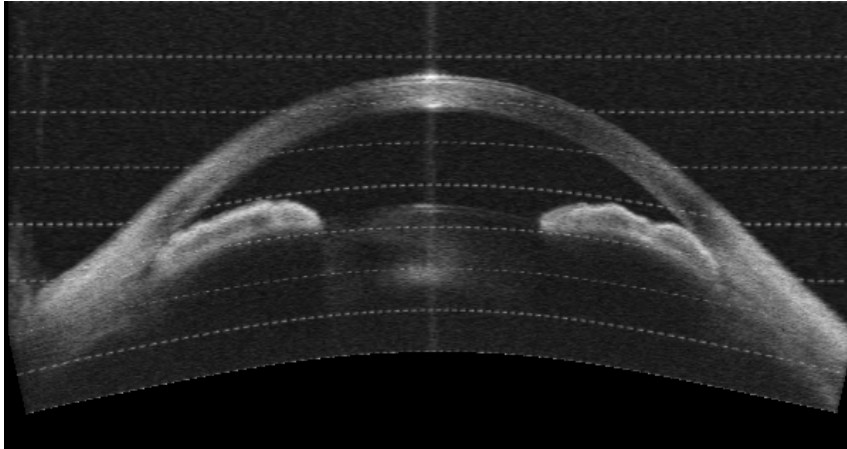
# Angle closure and the lens



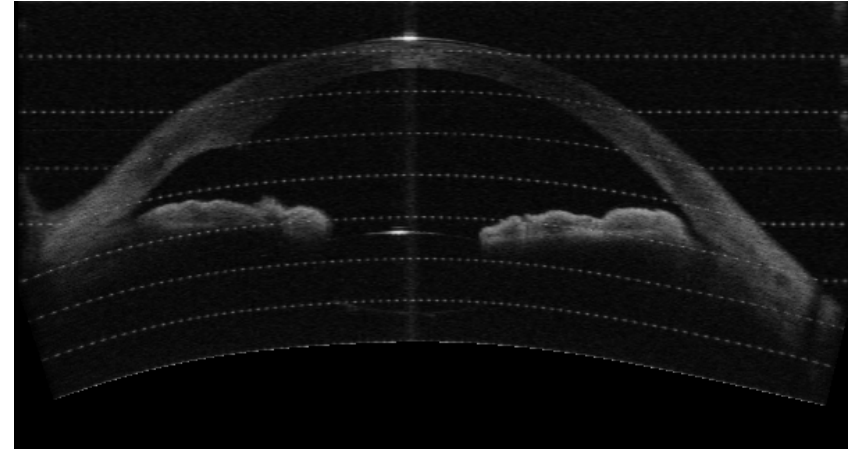
# Lens vault



# Impact of lens extraction

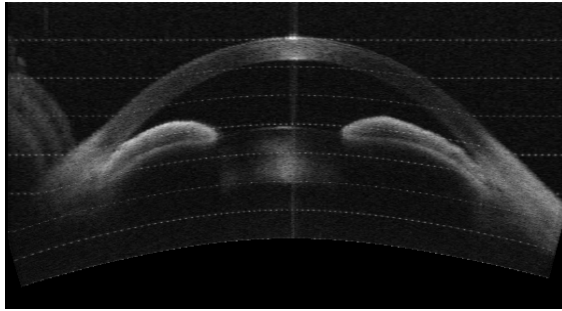


Pre - CE

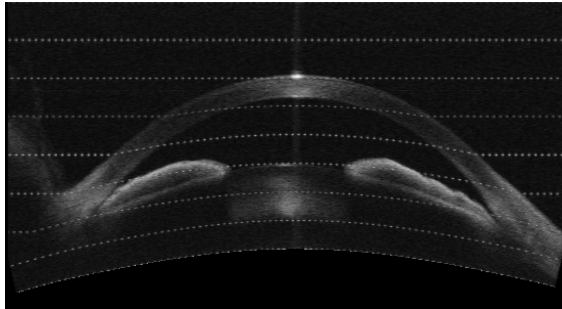


Post - CE

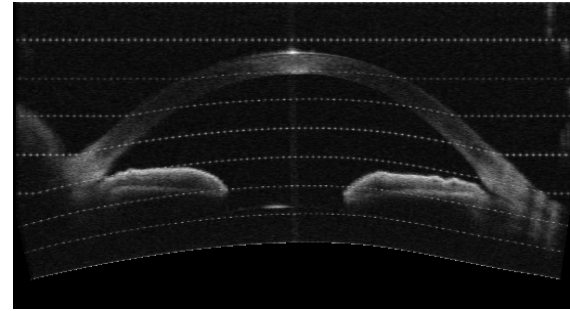
# Lens is a major factor



**Angle-Closure**

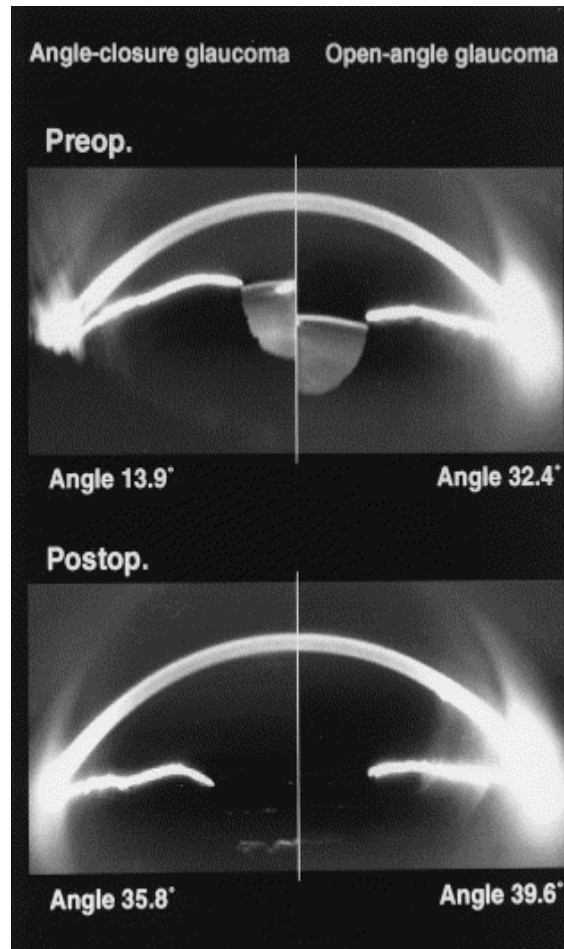


**Post-PI**

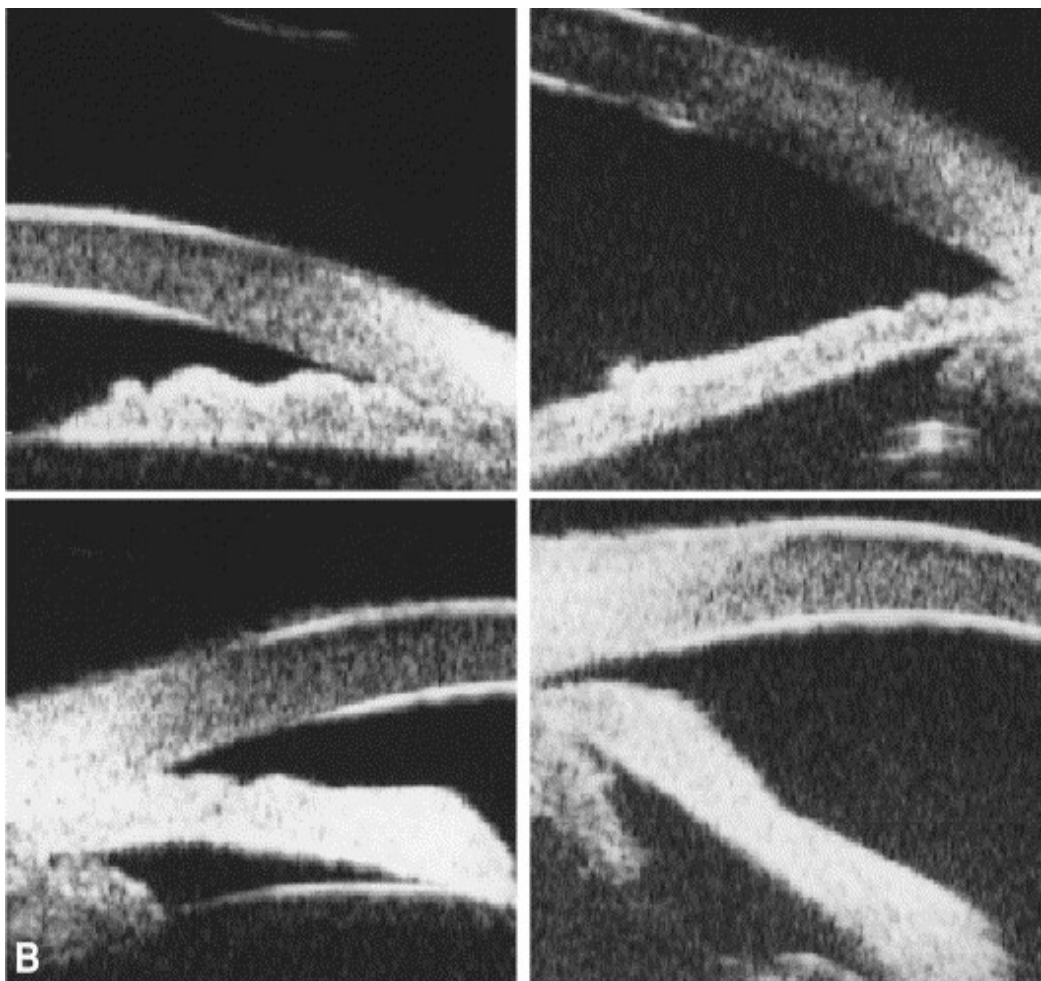


**Post-CE**

# Cataract Extraction



Hayashi,  
Ophthalmology 2000



Nonaka, Ophthalmology, 2005

# Acute Angle Closure Attacks

# Contralateral eye in AAC

≈ 10% present with bilateral disease

≈ 50% have an acute attack in the contralateral eye if untreated

Contralateral involvement within days

**Perform PI as soon as possible**

# Laser gonioplasty for AAC

Acute laser gonioplasty + medicines

9 consecutive patients

Mean of **66 mmHg** to **18 mmHg** in one hour

Lai JS, Tham CC, Chua JK, Lam DS. J Glaucoma 2001 Apr;10(2):89-94



# Paracentesis for AAC

10 eyes, 8 patients

Mean of **66 mmHg** to **15 mmHg**  
immediately after paracentesis

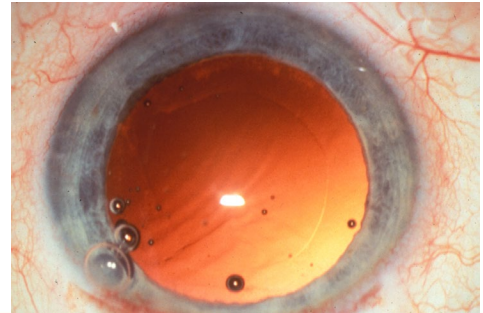
Lam DS, Chua JK, Tham CC, Lai JS, Ophthalmology 2002 Jan;109(1):64-70

# Acute angle closure and CE

Mean IOP = 40 mmHg in both groups, surgical iridectomy versus PECE

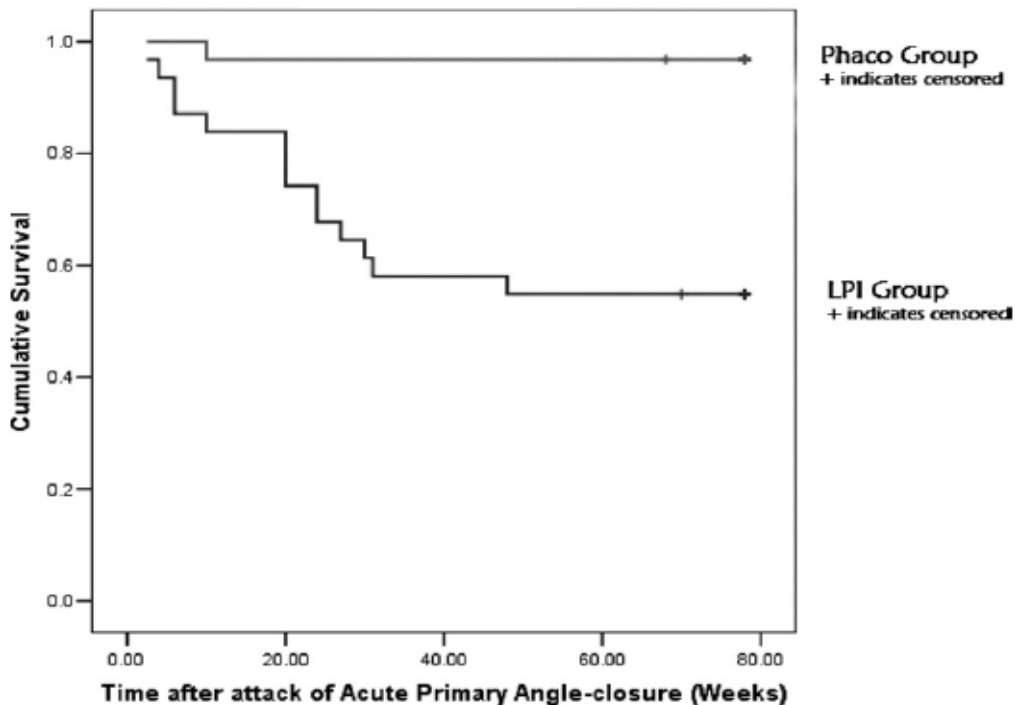
**63%** of iridectomy eyes versus **11%** of PECE eyes required **additional IOP-lowering surgery**

Jacobi, Ophthalmology, 2002



# Acute angle closure and CE

**Failure = IOP > 21 off medications**

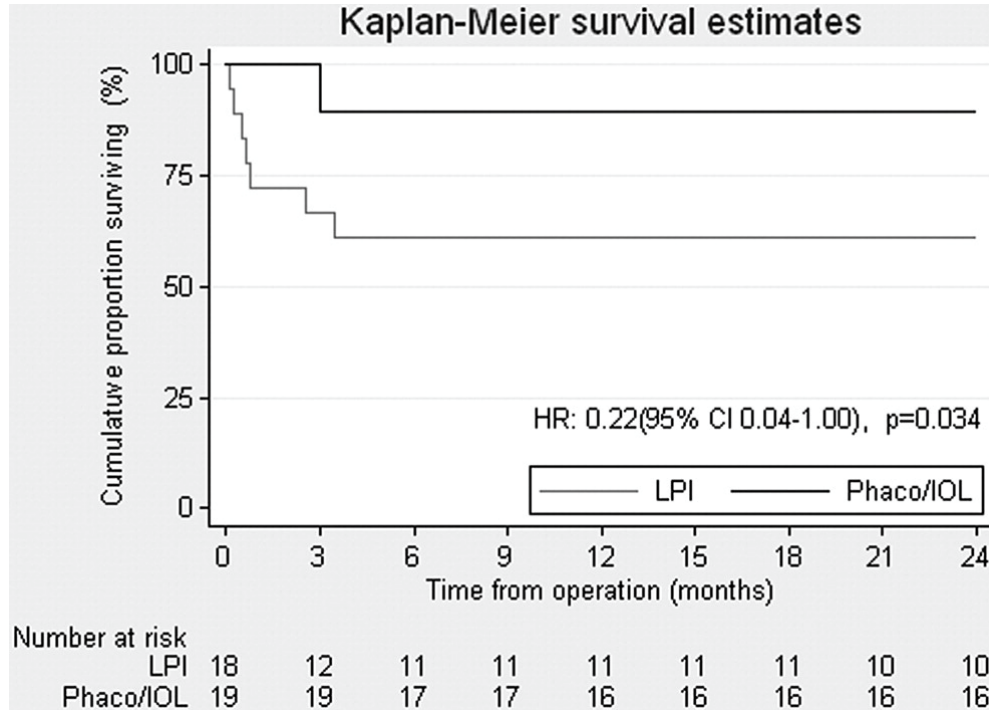


**HR = 14** LPI vs Sx

Lam DS, et al, Ophthalmology 2008

# Acute angle closure and cataract surgery

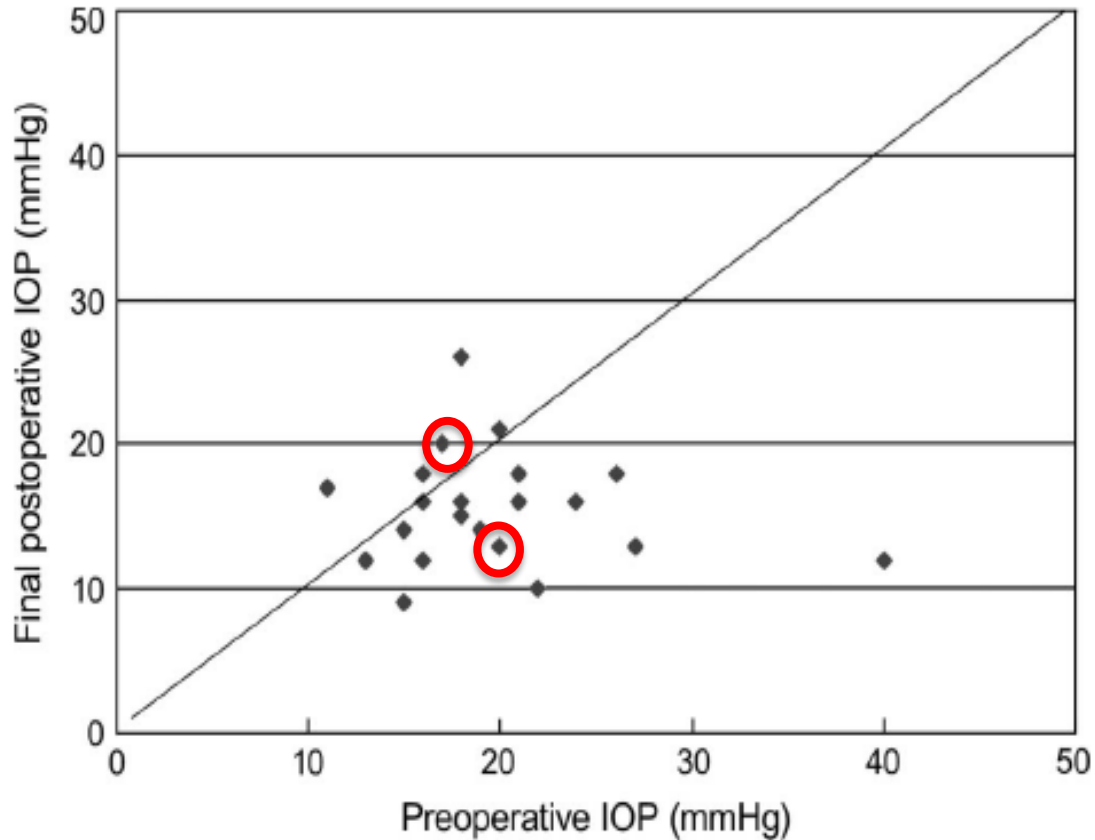
**Failure = IOP 22 – 24 two occasions or  $\geq 25$**



**HR = 4.5** LPI vs Sx

Husain, Ophthalmology, 2012

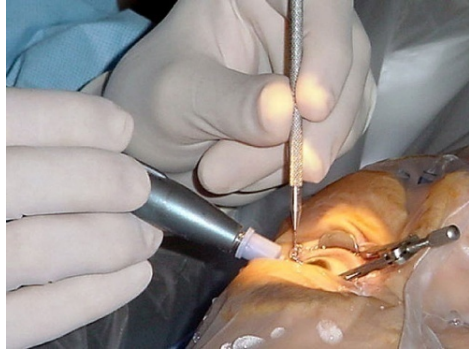
# Chronic angle closure



Lai, JOG, 2006



# Design: pragmatic RCT



PAC with IOP > 30 mmHg or PACG

**Phaco**

**Laser iridotomy**



If **both eyes eligible** both received the **same intervention**  
Index eye: the one with more advanced disease

**Follow-up = 3 years**

# Inclusion criteria

**PACG** with IOP  $\geq$  21 or **PAC** with IOP  $\geq$  30 mmHg

At least 180 degrees of angle closure

**Newly diagnosed** (up to 6 months)

Age  $\geq$  50 years

# Exclusion criteria

Previous diagnosed acute angle closure attack

**Severe glaucoma** (CDR  $\geq$  0.9 or MD  $\geq$  15 dB)

Symptomatic **cataract** in either eye

Axial length  $\leq$  19 mm (**nanophthalmos**)

Previous surgery (IOL, laser iridotomy)

**Increased surgical risk:** e.g., corneal opacity, Fuch's endothelial dystrophy, PXF, not able to be positioned to undergo standard technique



# Primary outcomes

**Patient-centred:** Health status (EQ-5D)

**Dimensions:** mobility, self-care, usual activity, pain/discomfort, and anxiety/depression

(Each dimension with **three levels:** ‘no problems’, ‘some problems’, ‘extreme problems’)

**Clinical:** IOP

**Economic:** Incremental cost per QALY

UK – 23 sites



Asia – 7 sites



Australia – 1 site



# Baseline characteristics (n=419)

**Race:** **29%** Chinese

**Age:** 67.0 (+/- 9.8) years

**Diagnosis:** **PAC** = 37%, **PACG** = 62%

**IOP:** **28.9** (+/- 9.7) mmHg

**MD:** -4.2 (+/-6.0) dB

# Primary outcome: EQ-5D

EQ-5D score		Lens extraction		Laser PI	
		mean (SD)		mean (SD)	

Baseline	204	0.87	204	0.88
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<b>36 months</b>	176	<b>0.87</b>	175	<b>0.84</b>
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# Primary clinical outcome: IOP

		<b>Lens extraction</b>		<b>Laser PI</b>
<b>IOP (mmHg)</b>		mean (SD)		mean (SD)

Baseline	208	29.5	211	30.3
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<b>36 months*</b>	182	<b>16.6*</b>	184	<b>17.9*</b>
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\*Includes patients who had glaucoma surgery during the 3-year follow-up

# Medications at 36 months

# of medications*	Lens Extraction*	Laser PI*
0	126 (60.6%)	45 (21.3%)
1	33 (15.9%)	67 (31.8%)
2	15 (7.2%)	46 (21.8%)
3	3 (1.4%)	19 (9.0%)
4	1 (0.5%)	4 (1.9%)
<b>Mean <math>\pm</math> SD*</b>	<b>0.4 <math>\pm</math> 0.8*</b>	<b>1.3 <math>\pm</math> 1.0*</b>

\*Includes patients who had glaucoma surgery during the 3-year follow-up

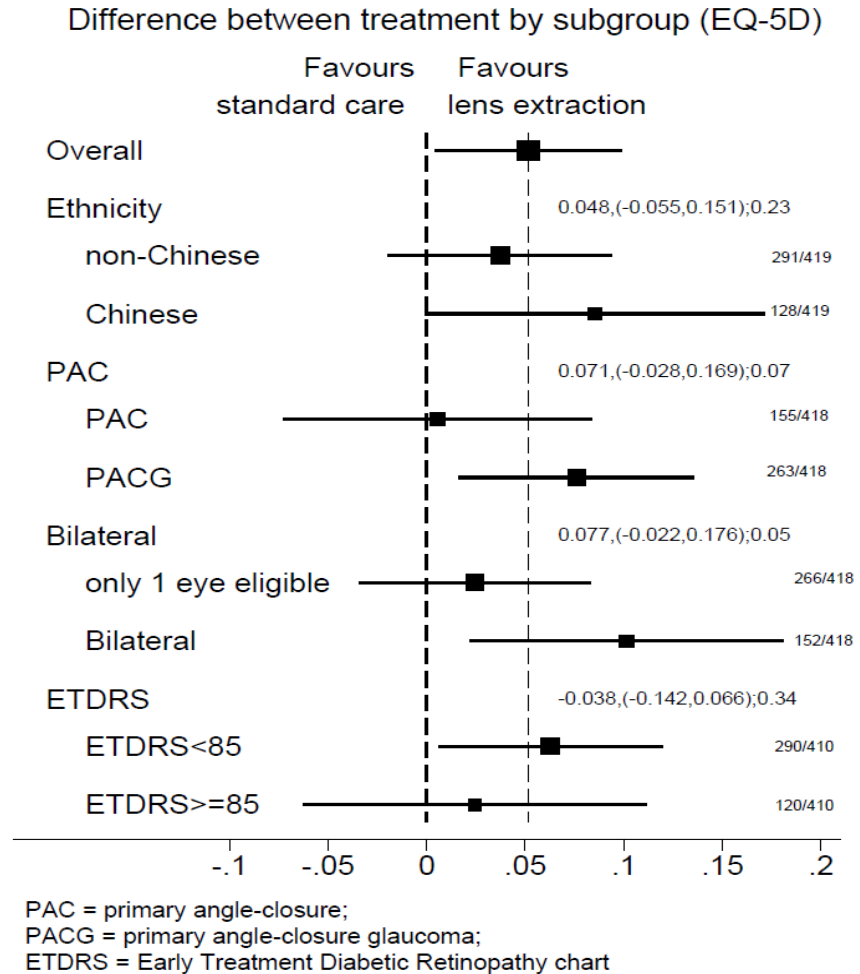
<b>Glaucoma Surgery</b>	<b>Lens extraction N=208</b>	<b>Laser PI N=211</b>
<b>Lens Extraction</b>		16
<b>Trabeculectomy</b>	1	6
<b>i-Stent</b>		1
<b>Ahmed tube</b>		1
<b>TOTAL</b>	<b>1</b>	<b>24</b>
<b>Cataract surgery for reduced vision</b>	<b>n/a</b>	<b>12</b>

# Surgery for complications and vision loss

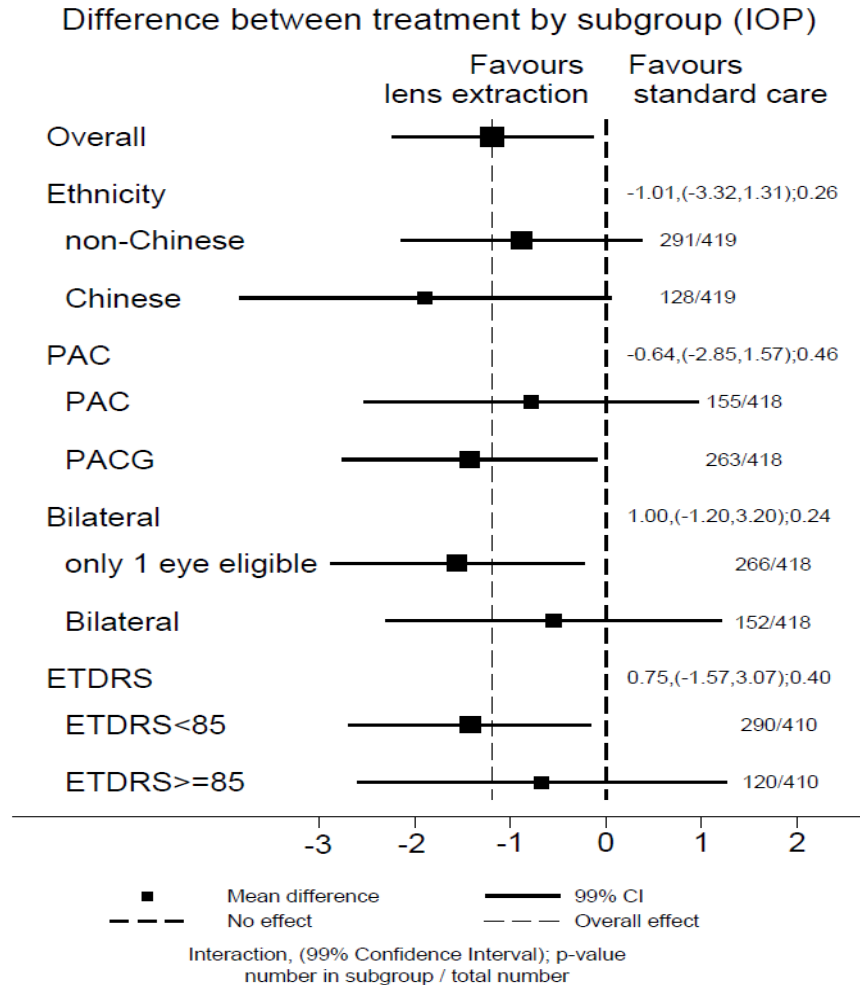
	<b>Lens extraction (N=208)</b>	<b>Laser PI (N=211)</b>
<b>Intra-ocular surgery required for complications</b>	<b>3 (1.4%)</b> Zonulo-hyaloido-vitrectomy for malignant glaucoma Repositioning of a subluxated IOL Injection of anti-VEGF for macular oedema	<b>1 (0.5%)</b> Pars plana vitrectomy for dislocated lens
<b>Irreversible loss of &gt;10 ETDRS letters</b>	<b>1 (0.5%)</b>	<b>3 (1.4%)</b>



## Difference in EQ-5D by sub-groups



# Difference in IOP by sub-groups



# IOP outcome

Target 15 – 20 mmHg

Increase or decrease in medication determined by physician, if IOP not controlled, surgery could be offered

**Good responder:** IOP < 21  
mmHg and no surgery

**Great responder:** IOP < 21, no  
surgery and no medications

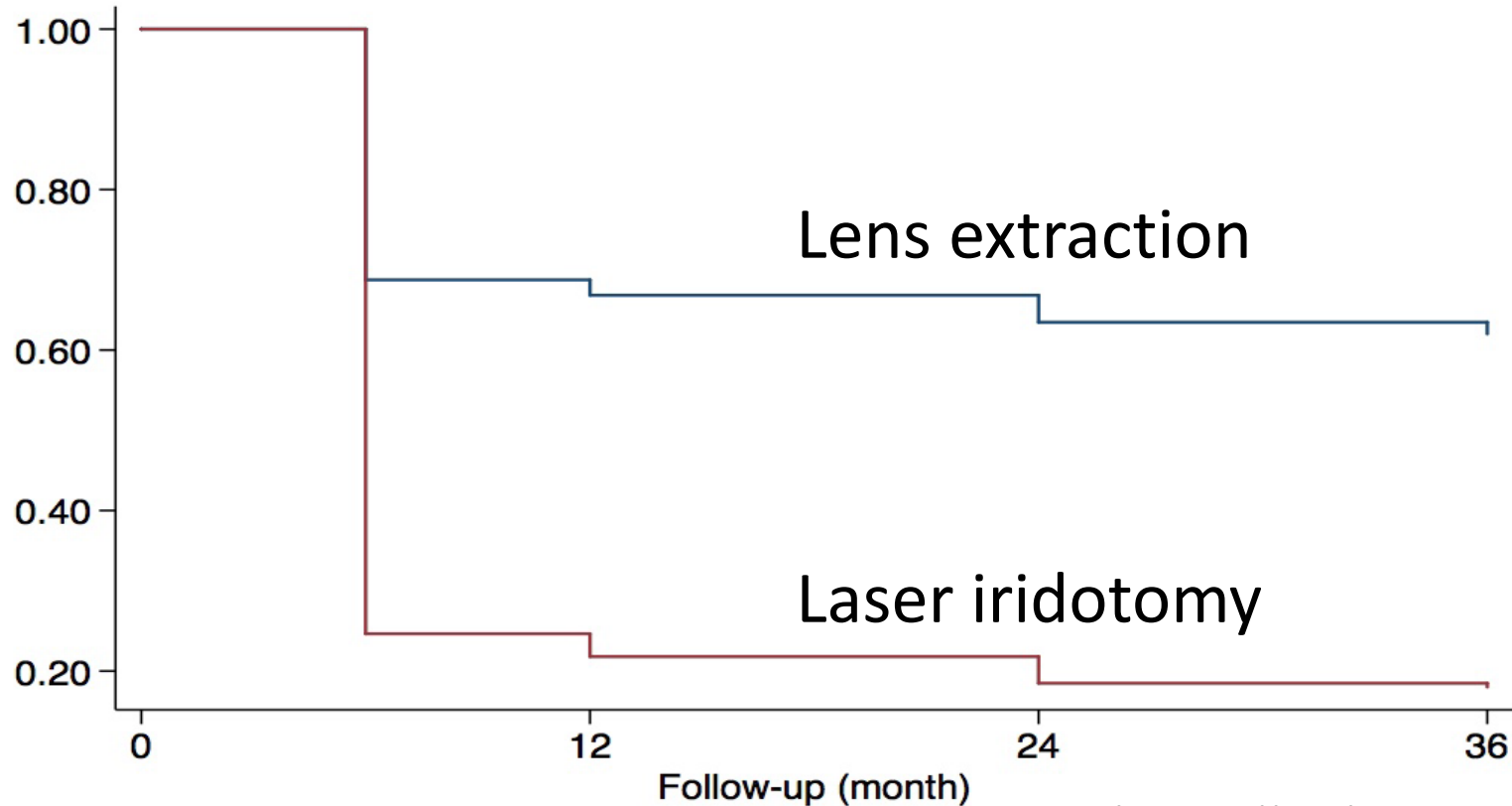
# IOP control at 36 months

	CLE	LPI
<b>Good response</b>	163 (89.6%)	125 (66.8%)

# IOP control at 36 months

	CLE	LPI
<b>Good response</b>	163 (89.6%)	125 (66.8%)
<b>Great response</b>	120 (63.9%)	33 (17.7%)

# “Great response” survival curve



Log rank test for equality of failure function: p-value<0.001

# Cost-effectiveness

ICER = £14,284 per QALY gained for lens extraction versus laser PI at 3 years

(NHS perspective, based on 285 UK participants)



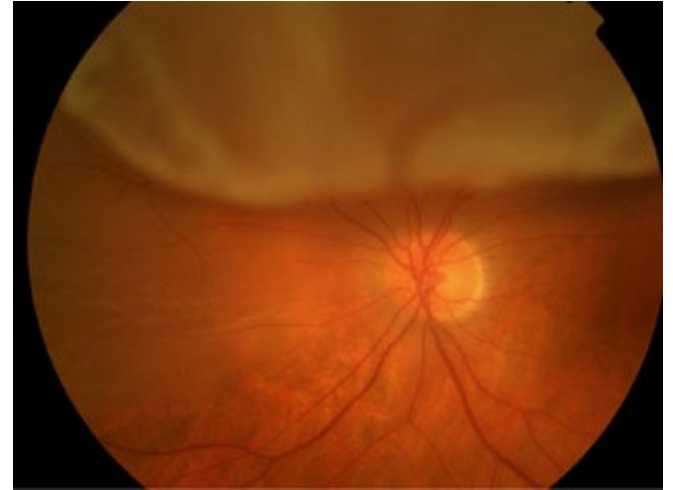
# Cataract surgery is not without risk

1% retinal detachment

2% CME

One in two thousand cases of endophthalmitis

Others



# Conclusion from EAGLE

**Initial lens extraction is associated with better clinical and patient-reported outcomes than LPI**

Initial lens extraction is cost-effective

Lens extraction has a risk of PC rupture: individualized decision making!

EAGLE results not applicable to other types of PACs/PACGs

*Azuara-Blanco, Burr, Ramsay, Cooper, Friedman...Lancet, 2016*

What about those with angle closure without disease?

# Population Over 50 in China

2005  $\approx$  290 million

2050  $\approx$  641 million

**What should we do about all those with PACS???**

# Chennai glaucoma study

278 PACS

106 PAC

34 PACG

**< 10% with real disease**

# Natural history after PI?



# Population characteristics

62 years old at time of attack

68% female

87% Chinese

Mean f/u 6.3 years (range 4 – 10)

# Attack eyes

43 (48%) eyes had glaucoma

Average MD = - 11

18 eyes felt to have pallor in excess of  
cupping on photographic review

Aung, Friedman, et al, Ophthalmology, 2004



**10% of attack eyes were  
blind from glaucoma**

# Contralateral eyes

Only 4 eyes out of 76 developed glaucoma over follow up (**5%**)

3 had nerve findings only, no VF loss (probable cases)

# Avoiding acute attacks makes sense

APAC attacks result in **severe vision loss**  
in a substantial proportion of attack eyes

Contralateral eyes **do well** after iridotomy



# Laser PI can have adverse outcomes

Blood-aqueous-barrier disruption

Acute IOP rise

Burns of the cornea, lens and retina

Glare and diplopia

? Cataract    ? Endothelial cell loss

# LPI to prevent angle closure

- Guangzhou, Southern China
- Screened over 10,000 people for narrow angles
- Enrolled 889 subjects
- Randomized one eye to laser PI
- Completed 6 years follow-up

# Composite endpoint

IOP > 24 mmHg on two separate occasions; **OR**

PAS of at least one clock hour; **OR**

Acute angle closure

# LPI reduced endpoints, but rates were low

	LPI (n=889)	Control (n=889)	<i>p</i>
Composite endpoint	n=19 4.2/1000 EY	n=36 8.0/1000 EY	0.02



# LPI reduced endpoints, but rates were low

	LPI (n=889)	Control (n=889)	<i>p</i>
<b>Composite endpoint</b>	<b>n=19</b> <b>4.2/1000 EY</b>	<b>n=36</b> <b>8.0/1000 EY</b>	<b>0.02</b>
IOP>24 mmHg	n=3	n=5	0.48
PAS≥1 clock hour	n=15	n=30	<b>0.02</b>
Acute attack	n=1	n=5	0.10

# Acute attacks

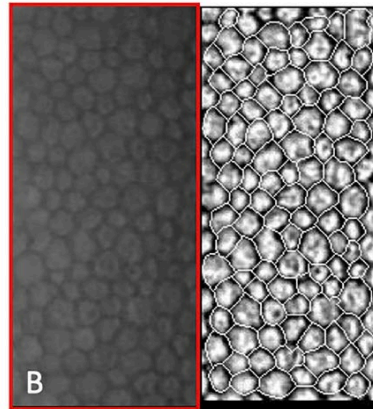
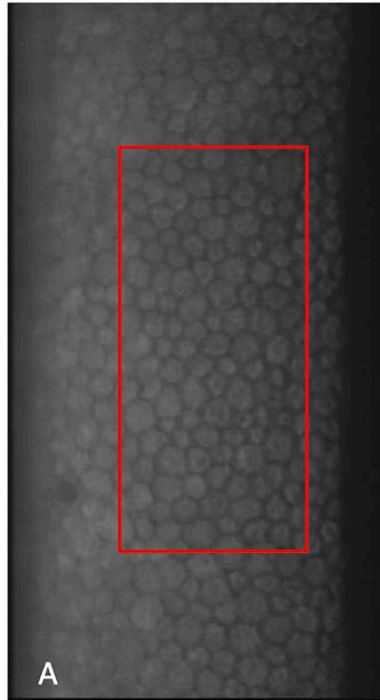
Three control eyes and one LPI-treated eye had acute attacks **after dilation**

**6.3 AAC cases per 10,000 dilations in control eyes**

Only **two attacks** occurred (both in untreated eyes) outside of dilation

**4.4/10,000 eye-years** in untreated eyes if dilation-induced cases are excluded

# Central endothelial changes over time



- cell count density (ECD)
- size and % hexagonality
- avg of about 90 cells per image

Liao, BJO, 2020

# No serious adverse events

	LPI (n=889)	Control (n=889)
<b>Immediate Post-LPI</b>		
Localized hyphema	n=257 (29%)	
Localized corneal burn	n=1 (0.1%)	
IOP $\geq$ 30mmHg	n=6 (0.7%)	
<b>72 months</b>		
Endothelial cell density	2470 $\pm$ 308	2485 $\pm$ 306
Cataract LOCS III	2.9 $\pm$ 0.8	2.8 $\pm$ 0.7

# Central endothelial changes over time

Cases **4.9% reduction in ECD versus 4.2%** in controls

Hexagonality, size changed, but similar between groups

LPI parameters **not associated** with rate of ECD decline

Liao, BJO, 2020

# Overall conclusions

**LPI was protective**, but mainly against interim outcomes (mostly PAS)

Most cases of acute attack were following dilation, **two control eyes over 6 years had AAC**

**We may be doing too many LPIs**









# Overall major conclusions

Acute attack eyes should have **lenses removed** after the attack

Fellow eyes should have LPI **right away**

**EAGLE** should change the paradigm for treating PACG

**ZAP** has shown that not everyone needs an iridotomy