

A Case for Re-defining the Intraocular Pressure Referral Threshold: Findings from the UK Biobank

Michelle P Y Chan ¹, Carlota Grossi Sampedro ¹, Stephen A Vernon ², James E Morgan ³, Praveen J Patel ¹, Peng T Khaw ¹, Paul J Foster ¹

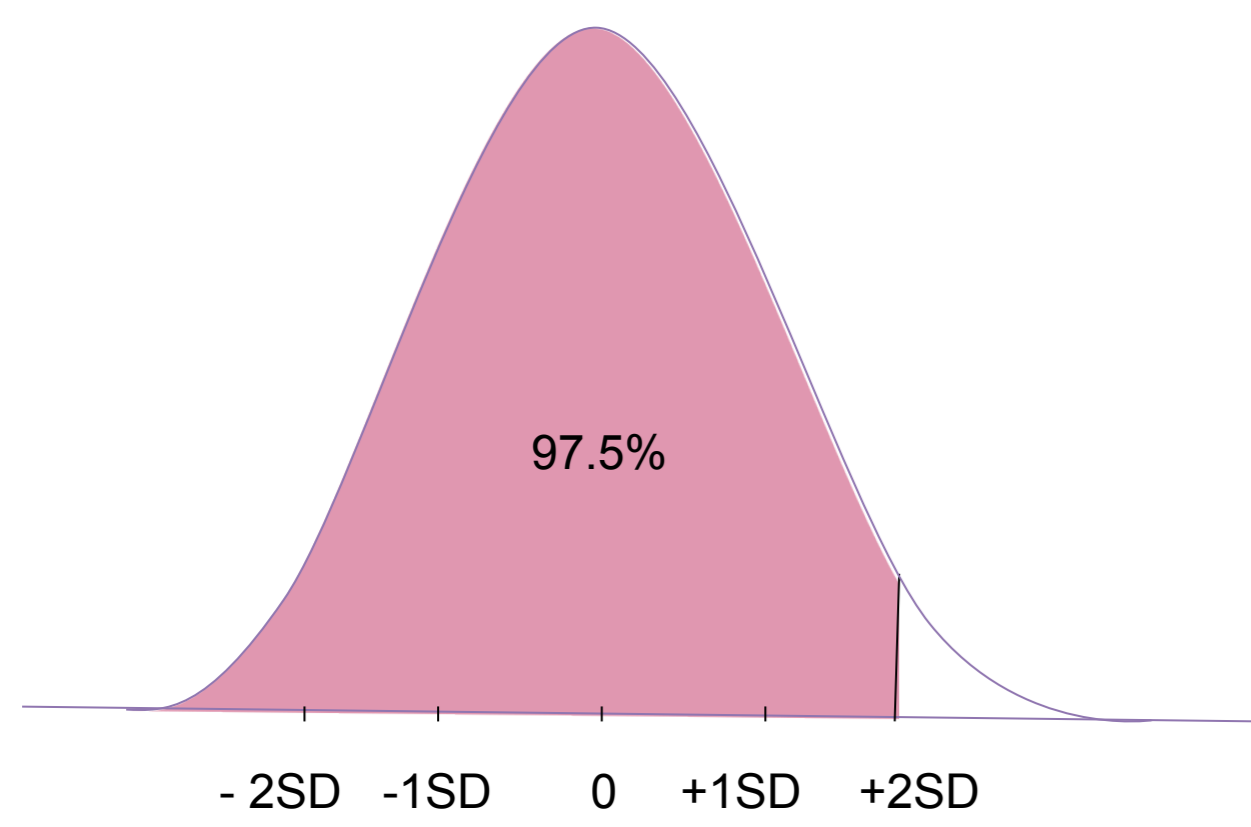
¹ Moorfields Eye Hospital NHS Foundation Trust ² Nottingham University Hospitals NHS Trust ³ School of Optometry and Vision Sciences, Cardiff University

Introduction

- The conventional definition of ocular hypertension is intraocular pressure (IOP) >21mmHg
- In 2010, UK optometrists were advised in official guidelines to refer anyone with IOP >21mmHg in either eye to the hospital eye service even without additional risk factors.¹ This sharply increased hospital referrals by a third² without improving the diagnostic yield.³
- Most optometrists base their referrals on non-contact tonometry (NCT)⁴

The Origin of 21mmHg

- It was derived from a 1966 population survey conducted in Rhondda Valley, Wales, using Goldmann applanation tonometry (GAT).⁵
- 21mmHg corresponds to the study populations' mean IOP + 2 standard deviations (SD). IOP ≤ 21mmHg therefore includes 97.5% of the population's IOP values, assuming the IOP distribution to be Gaussian. It has since been widely adopted as the upper limit of "normal" IOP.



Why is >21mmHg no longer relevant to current referral practices?

- 21mmHg was originally derived using applanation tonometry data, while most optometrists base their referrals on NCT measurements.
- The mean+2SD threshold value varies across different populations due to differences in age, sex and ethnicity, and possibly other physical & environmental factors. The mean+2SD in a UK population today may not be the same as that in Wales in 1960s.

Aims

- To determine the IOP referral threshold (mean +2SD) measured with a non-contact tonometer in the UK Biobank cohort
- To estimate the impact of varying the IOP referral threshold on referable numbers to the Hospital Eye Service

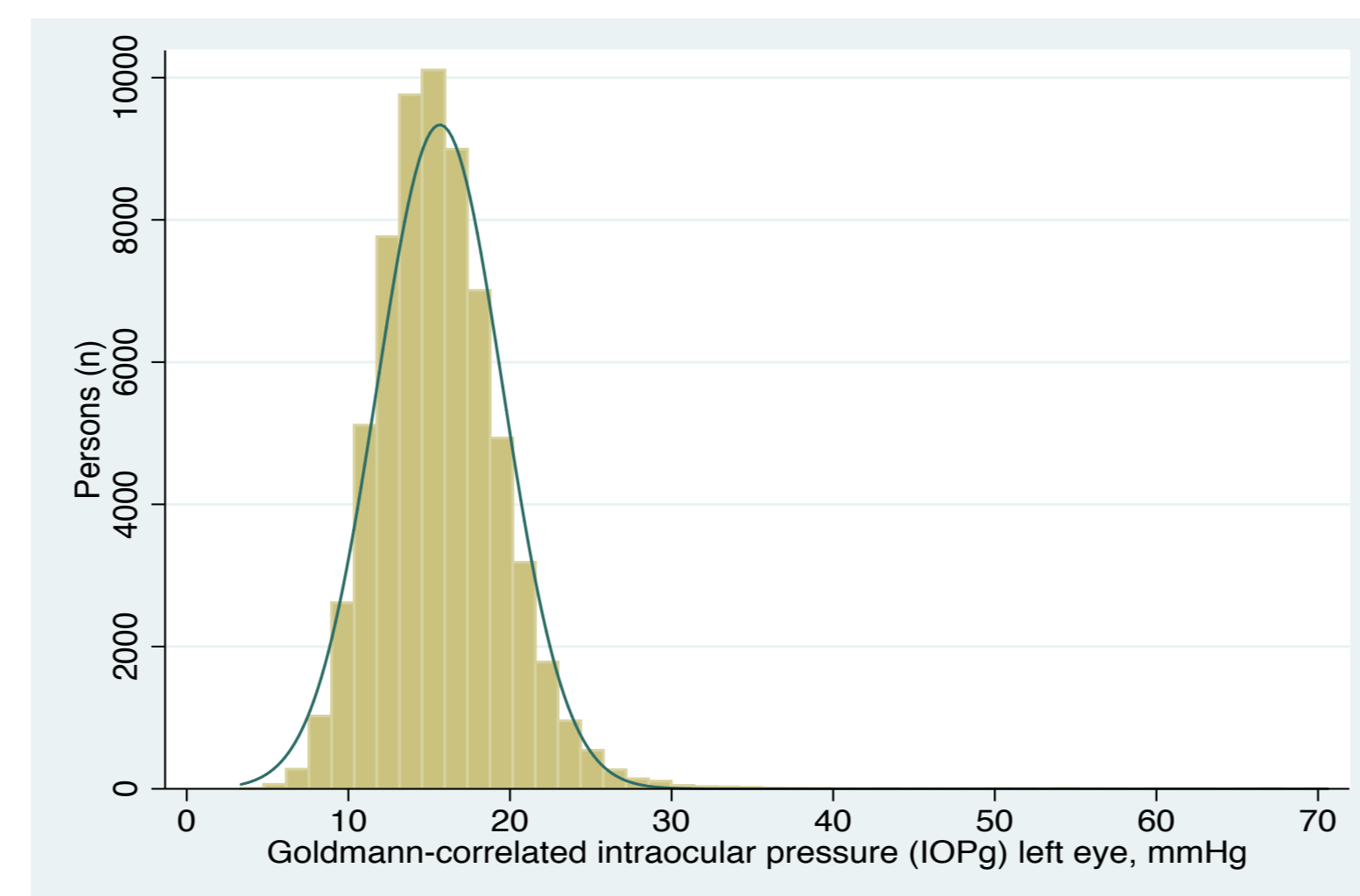
Acknowledgements The authors would like to thank Andrew Elders, Jonathan Cook and Jennifer Burr for sharing unpublished findings on tonometer agreements.

Funding The UK Biobank was established by the Wellcome Trust Medical charity, Medical Research Council, Department of Health Scottish Government, and the Northwest Regional Development Agency.

References 1) Association of British Dispensing Opticians, Association of Optometrists & Federation of Ophthalmic & Dispensing Opticians. 24 April 2009, updated 11 Feb 2010. Available: http://www.aop.org.uk/uploads/uploaded_files/glaucoma_faqs_6th_revision_11-02-2010.pdf 2) Edgar, D., Romanay, T et al 2010. *Optometry in Practice*, 11, 33-38 3) Shah, S. & Murdoch, I. E. 2011. *Ophthalmic Physiol Opt*, 31, 339-42. 4) Myint, J., Edgar, D. F. et al. 2011. *Ophthalmic Physiol Opt*, 31, 353-9. 5) Hollows, F. C. & Graham, P. A. 1966. *Br J Ophthalmol*, 50, 570-86. 6) Cook, J. A., Botello, A. P. et al 2012. *Ophthalmology*, 119, 1552-7. 7) Tielsch, J. M., Katz, J. et al 1991. *Am J Epidemiol*, 134, 1102-10.

Results

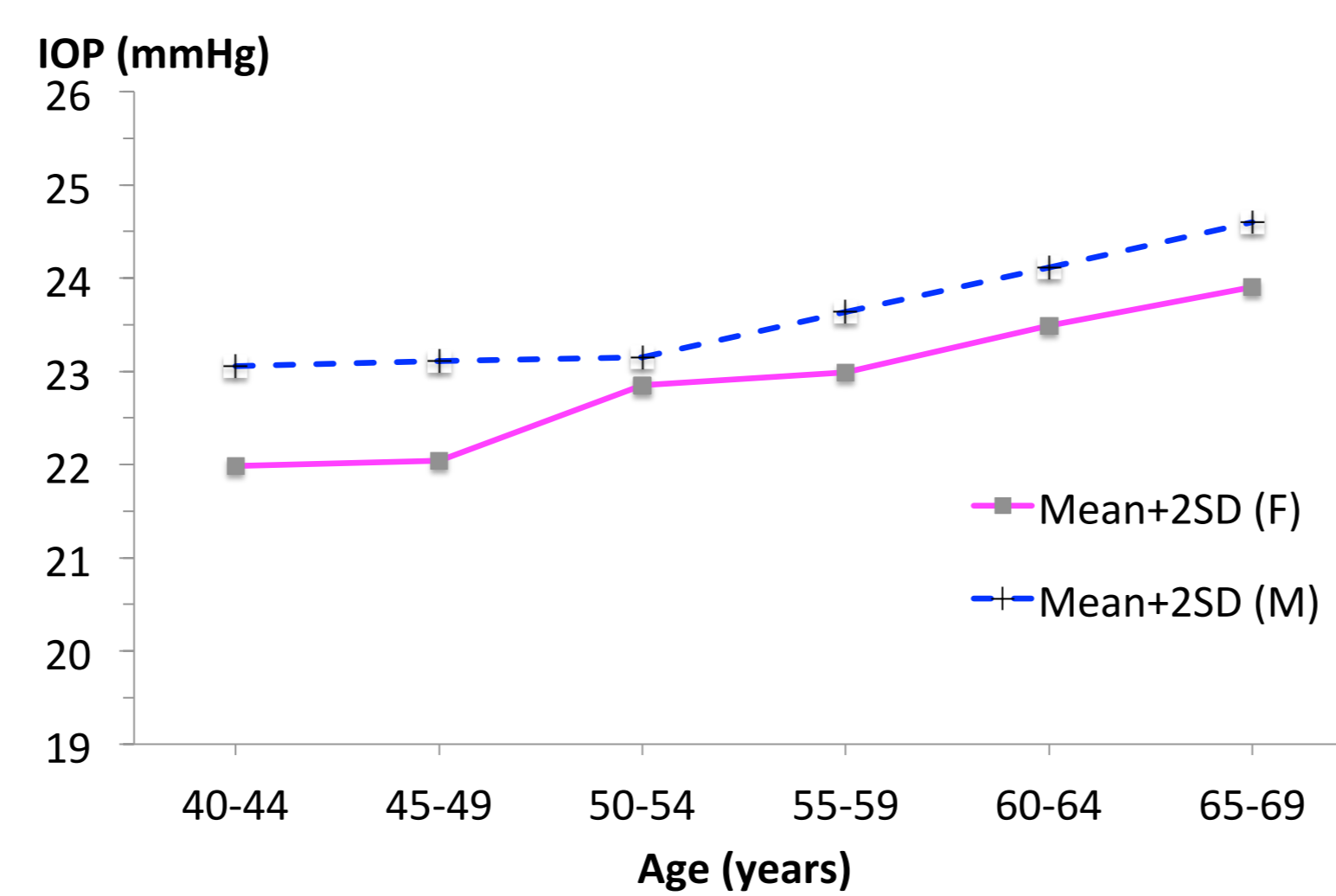
- IOPg data were available for 65,026 participants (mean age 57.4 years, 54.3% women, 90.7% White ethnicity).
- The study populations' mean IOPg was 15.7mmHg (SD 3.9mmHg, 95% CI 15.6-15.7mmHg).



Left eye IOPg distribution in the UK Biobank cohort follows a normal distribution with a right skew

Referral thresholds (mean IOP+2SD) by age and sex

- The overall mean+2SD for the study population was 23.6mmHg. The 97.5th centile IOP was 23.7mmHg.
- The age-specific mean IOP+2SD for men varied between 23.1-24.6mmHg, for women it varied between 22.0-23.9mmHg.



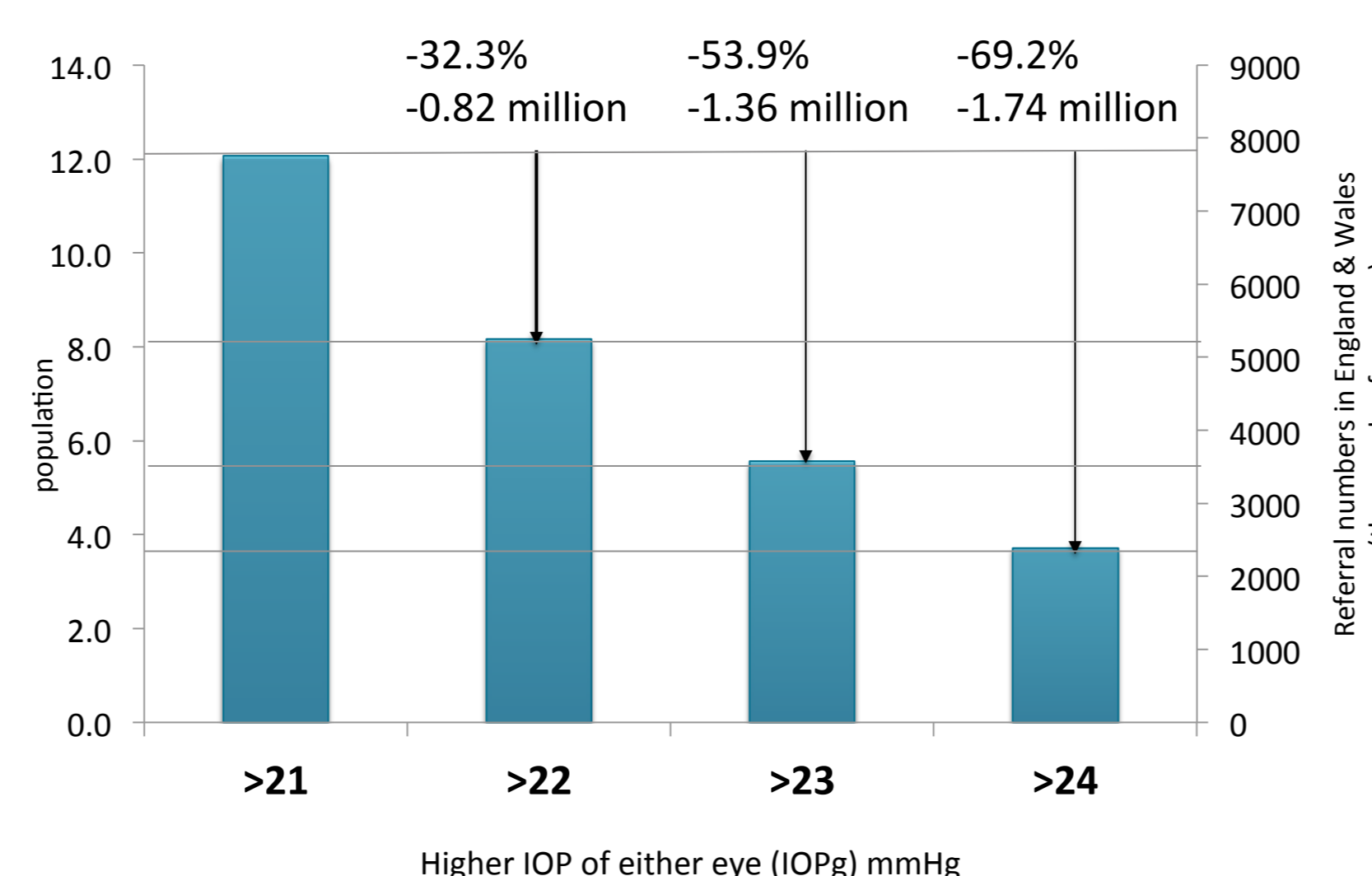
Effects on projected referable cases in England and Wales

Raising the referral threshold from >21mmHg to >24mmHg would reduce the number of referable subjects by 69.2% (1.74 million persons).

Even a modest increase to >22mmHg would reduce the number of referrals by 32.3% (0.82million persons).

New referral threshold	Change in persons eligible for referral	
	%	persons (million)*
>22mmHg	-32.3	-0.82
>23mmHg	-53.9	-1.36
>24mmHg	-69.2	-1.74

* Applied to age-matched population of England and Wales (2011 census)



Methods

Design Population based cross-sectional multi-site cohort study: the UK Biobank.

Participants All British residents aged 40-72 registered with the NHS were invited to join the UK Biobank between 2006 – 2010 if they live within 25 miles from one of twenty-two recruitment centres.

In this study, data of participants recruited from six assessment centres (Birmingham, Hounslow, Croydon, Sheffield, Liverpool and Swansea) were available for analysis.

Measurements A single IOP measurement was taken on each eye using the Ocular Response Analyser (ORA), a non-contact tonometer. Goldmann-correlated IOP (IOPg) in the left eye was used in all analyses.

Outcome measures

- Referral thresholds (mean IOP + 2SD) by age and sex
- Projected numbers of referable cases at different IOP levels (using the maximum IOP of either eye, applied to age-matched population of England and Wales based on 2011 census data)

Discussion

Why is our mean+2SD higher than 21mmHg?

Compared to other studies of white populations' IOP measured with GAT, our IOP data have the largest standard deviation. This is most likely related to the use of NCT, and that only one IOP measurement was used.

Location	n	Age	Method	Mean (SD) mmHg	Mean +2SD mmHg
UK Biobank	65,026	40-69	ORA	15.7 (3.9)	23.6
EPIC-Norfolk	7903	48-92	ORA	16.1 (3.9)	23.9
Baltimore	2913	>40	GAT	17.2 (3.4)	23.9
Thessaloniki	2554	>60	GAT	15.3 (3.5)	22.3
Beaver Dam	4926	43-86	GAT	15.3 (3.4)	22.1
Wales (1966)	1873	>40	GAT	15.9 (2.9)	21.6
Blue Mountains	3654	>49	GAT	16.0 (2.6)	21.2

Applicability of results

- The applicability of our findings depends on how ORA IOPg values agree with conventional NCTs, used by most optometrists.
- A recent systematic review of tonometers agreement showed that conventional NCT measurements are higher than GAT by 0.2mmHg.⁶ IOPg values are higher than GAT by 1.3mmHg (personal communications, Dec 2013). It can be inferred that IOPg measurements are higher than conventional NCT by 1.1mmHg.
- By subtracting 1.1mmHg from each measurement in this study, the newly corrected mean+2SD is 22.3mmHg still higher than 21mmHg.

Implications of a higher IOP referral threshold

Missed treatment for raised IOP is unlikely According to NICE guidelines, the IOP at which treatment is required for ocular hypertension starts at 25mmHg. Increasing the referral threshold up to 24mmHg is unlikely to have a detrimental effect of missed treatment.

Increase specificity for open-angle glaucoma detection Fewer false positive referrals will bring substantial financial savings to the NHS.

Reduce sensitivity for open-angle glaucoma detection More glaucoma cases will be missed. However, no single IOP value provides a good trade-off between sensitivity and specificity of open-angle glaucoma detection⁷ and IOP alone should not be used as a screening tool for glaucoma without considering other risk factors.

Conclusions

The study population's mean IOP+2SD measured with an NCT was 23.6mmHg, higher than the conventional referral threshold of 21mmHg. This study makes a strong case for increasing the non-contact IOP referral threshold in patients without additional glaucoma risk factors.