HRA Protocol Compliance Declaration

This protocol has regard for the HRA guidance and order of content

AN EXAMINATION OF NEW VISUAL ACUITY AND CROWDING DISTANCE TESTS,

FOR BETTER DETECTION OF AMBLYOPIA.

New visual acuity and crowding tests for better detection of amblyopia.

PROTOCOL VERSION NUMBER: 5.0

DATE: 17/02/2021

IRAS Number: 238449

Sponsor number: FST/FREP/17/739

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: ..... Date: ...../...../.....

Name (please print):

.....

Position: .....

Chief Investigator:

Signature: ..... Date: ...../...../.....

Name: (please print):

.....

Research Supervisor:

Signature: ..... Date: ...../...../.....

Name: (please print):

.....

LIST OF CONTENTS

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Sponsor	Anglia Ruskin University Contact on behalf of the Sponsor Professor Peter Bright Chair: FREP (Faculty of Science and Technology Research Ethics Panel) Department of Psychology, Faculty of Science and Technology, Anglia Ruskin University, Cambridge CB1 1PT Phone: 01223 698647 peter.bright@aru.ac.uk
Joint-sponsor(s)/co-sponsor(s)	N/A
Funder(s)	Contact on behalf of the Sponsor/funder Anglia Ruskin University (via The Doctoral School) Dr Alan White Director of Doctoral School Research and Innovation Development Office Anglia Ruskin University, Chelmsford CM1 1SQ Phone: 01245 684957 alan.white@aru.ac.uk

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Committees	FRDSC: Faculty Research Degrees Sub-Committee Professor Michael Cole – Deputy Dean (Research and External Income) Chair, Faculty of Science and Technology FRDSC SCI 712 Cambridge Phone: 01223 698525; michael.cole@aru.ac.uk Fax: 01223 417712 FREP – Faculty Research Ethics Panel Professor Peter Bright Chair, Faculty of Science and Technology FREP SCI 604 Cambridge Phone: 01223 698647 peter.bright@aru.ac.uk Fax: 01223 417712

STUDY SUMMARY

Study Title	An examination of new visual acuity and crowding distance tests for better detection of amblyopia.
Internal ref. no. (or short title)	New visual acuity and crowding tests for better detection of amblyopia.
Study Design	In this single centre study, assessment of three theoretical enhancements to visual acuity testing 1) crowding-enhanced letters, 2) crowded-enhanced contrast-modulated letters and 3) measurement of crowding distance, will be tested using clinical tests in a control group and in amblyopic children. Results from these 3 tests will be compared to each other and to those from the Sonksen logMAR Test (SLT) the current clinical standard, as measured by a clinician. Comparisons across test, and between participant groups, will enable us to determine the optimal test, or combination of tests, for detecting amblyopia. Visual acuities and crowding distance will be measured prospectively in a randomised controlled trial. Results will also be obtained in a control group, a sample of false-positive referrals to the hospital, and compared to that already obtained on normal healthy children (Waugh et al., 2018). The testing will take place in a clinical room neighbouring the ACPOS (Addenbrooke's Community Paediatric Ophthalmology Service) clinic, which is hosted within the University Eye Clinic at Anglia Ruskin University (ARU).
Study Participants	**Test participants;** 42 Male and female, 3 to 11-year-old children diagnosed as having amblyopia (21 strabismic and 21 anisometropic) by clinicians within Addenbrookes Community Paediatric Ophthalmology Service (ACPOS), hosted by the University Eye Clinic at Anglia Ruskin University (ARU) will be recruited. **Control Participants;** 21 Male and female, 3 to 11-year-old children who have either been falsely referred into ACPOS (Addenbrookes Community Paediatric Ophthalmology Service) by the national vision screening service, but who are subsequently found to have satisfactory visual function; or visually healthy volunteers who have already passed vision screening will be recruited. All participants must be able to perform the Sonksen logMAR Test (SLT) either verbally, or by using a matching card.
Planned Size of Sample (if applicable)	Total participant pool: *n*=63 Anisometropic amblyopes *n*=21; Strabismic amblyopes *n*=21; Control group *n*=21.

Follow up duration (if applicable)	This project requires one visit by each participant. However participants may choose to participate more than once (up to a maximum of 3 times) during the recruitment and testing period (within the 2 year data collection period).
Planned Study Period	It is planned that recruitment and testing will take place over 2 year period. (See Gantt Chart for estimated project delivery dates).
Research Question/Aim(s)	This study aims to investigate whether proposed modifications to visual acuity tests will offer better sensitivity to the detection of amblyopia than the Sonksen logMAR test (SLT). It will also determine whether differences in outcomes occur for anisometropic, versus strabismic amblyopes.

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
1) Anglia Ruskin University (via The Doctoral School) Dr Alan White Director of Doctoral School Research and Innovation Development Office Anglia Ruskin University, Chelmsford CM1 1SQ Phone: 01245 684957 alan.white@aru.ac.uk	The Research Supervisor/Chief investigator (Dr Sarah J Waugh) has been awarded a Vice Chancellor's Studentship to provide fees and a living stipend to support a PhD student, (Louisa Haine), throughout the course of this study.
2) Anglia Ruskin University via Quality Related Research Funds from HEFCE (Higher Education Funding Council for England) to FST and Anglia Vision Research. Professor Michael Cole Deputy Dean (Research and External Income) Faculty of Science and Technology Anglia Ruskin University CP1 1PT michael.cole@aru.ac.uk	Quality Related Research Funding from HEFCE awarded to ARU has been approved for the Research Supervisor to reimburse participants' parents/carers for their time (£10 per participation visit in the form of an amazon voucher) for this project. Quality Related Research Funding has been approved for the Research Supervisor to cover the cost of computer hardware and software required for the execution and analysis of data generated from this project.

Contact on behalf of the Sponsor

Professor Peter Bright,

Chair of Faculty of Science and Technology Research Ethics Panel (FST FREP),

Department of Psychology,

Faculty of Science and Technology,

Anglia Ruskin University,

Cambridge

CB1 1PT

Phone: 01223698647

ROLE OF STUDY SPONSOR AND FUNDER

The Sponsor and the Funder for this project is Anglia Ruskin University (ARU).

The Principle Investigator on this study is a PhD student (Louisa Haine) funded through an ARU Vice-Chancellor's PhD Studentship, awarded to the Chief investigator / Research Supervisor (Dr Sarah J Waugh). The award funds the PhD student's fees and bursary.

The study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results is the responsibility of the research student (The Principal Investigator) and the research supervisory team led by Dr Sarah J Waugh (The Chief Investigator /The Research Supervisor).

The Sponsor of this project, with regards to ethics approval, is the Chair of the Faculty of Science and Technology Research Ethics Panel, Professor Peter Bright.

The following relevant information with respect to student funding, the dissemination of research results and public engagement, has been taken from the "Anglia Ruskin University Vice Chancellor's PhD Studentships Terms and Conditions 2017-18 (Ver 2.0)".

Tenure of the studentship
Anglia Ruskin University expects studentship holders to maintain regular contact with their supervisors and other institutional authorities during the period of the award. The length of a studentship will not exceed three years. Continuation of all studentships is subject to the student's satisfactory annual progress. Funding for a student will cease once he or she has submitted their doctoral thesis, or reaches the end of the stated studentship duration, whichever is sooner.

Publication and Dissemination of Research
It is ARU policy that the results of the research it supports should be disseminated as widely as possible, for the benefit of other researchers and of the wider community (however, also see our statement regarding intellectual property rights below).

ARU has established arrangements for ensuring that these are deposited in our on-line repository and made available to other researchers. Students should consult their supervisors about those arrangements. Doctoral students should ensure that their thesis (or any other output such as an exhibition or performance) includes an acknowledgement of the support they have received from ARU.

Publication of any aspect of the research resulting from an ARU-funded studentship, through publications and other forms of media communication, including media appearances, press releases and conferences, must acknowledge the support received from the ARU.

Research students should discuss with their supervisors whether any or all of the results of their work should be published.

If a student, or anybody else, publishes any aspect of the research resulting from an ARU funded studentship, through publications and other forms of printed or electronic media

communication, including media appearances, websites, press releases and conferences, they must acknowledge the support received from ARU.

Learned societies and other organisations (such as the Institute of Historical Research) collect and publish information about doctoral theses completed and in progress. ARU strongly urges the submission of relevant information if asked to do so.

Exploitation and Intellectual Property Rights
ARU asserts the right to ownership of all intellectual property (IP) rights arising from research it funds through a VC PhD Studentship. A student should not enter into any agreement that may affect rights to exploit the IP arising from their work without first consulting the Director of RIDO (Research and Innovation Development Office of ARU).

Roles and Responsibilities for Project
It is up to the research student (The Principal Investigator) supervised by her Research Supervisor (and other members of the research supervisory team) under the auspices of the Faculty Research Degrees Sub-committee, to contribute to an approved study design and proposal. The study conduct, data analysis and interpretation, manuscript writing, and dissemination of results is also the responsibility of the research student (The Principal Investigator) in collaboration with her Research Supervisor (and other members of the research supervisory team) who are also in control the final decision regarding any of these aspects of the study.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT

COMMITTEES/GROUPS & INDIVIDUALS

Study Steering Groups

Information about research conducted by research students for a research degree is available in "Research Degrees Regulations" for Anglia Ruskin University found at: https://web.anglia.ac.uk/anet/academic/research_regulations.phtml .
Brief information about relevant study management groups is provided here.

Research Committee

The Research Committee is responsible for the development and implementation of Anglia Ruskin University's Research, Innovation and Knowledge Exchange Strategy.

Research Degrees Subcommittee (RDSC)

The Senate's Research Degrees Subcommittee (RDSC) is responsible, on behalf of the Research Committee, for the development of research degrees in Anglia Ruskin University and for developing, monitoring and reviewing Anglia Ruskin University's quality assurance and enhancement policies and procedures for monitoring and reviewing the quality of the student experience. Some of the Subcommittee's responsibilities and procedures are devolved to Faculty Research Degrees Subcommittees (FRDSCs).

Faculty Research Degrees Subcommittees (FRDSC)

FRDSCs monitor the progress of all research degrees students within the faculty and receive and approve documents relating to various key stages in a student's progress.

This proposed study has been approved by three reviewers, two with subject-specific expertise, from outside the Research Supervisory Team, but within the Faculty of Science and Technology, Anglia Ruskin University. The report by reviewers recommended (on 21/2/18) that the research proposal is approved by FRDSC, as being suitable for PhD level study. Approval will be ratified at the FRDSC meeting 3/5/18.

Research Ethics Subcommittee (RESC)

This Subcommittee of the Research Committee considers policies and procedures relating to the ethics of research investigations involving human participants, human tissue and organs, animals and other research that presents ethical issues undertaken by staff and students of Anglia Ruskin University. Responsibility for the approval of individual research ethics applications is devolved by Research Ethics Subcommittee to Faculty Research Ethics Panels.

Doctoral Supervisors for the Proposed Study

First Supervisor – Dr Sarah J Waugh (Anglia Vision Research)

Second Supervisor – Dr Monika A Formankiewicz (Anglia Vision Research)

Third Supervisor – Dr Akash S Chima (Anglia Vision Research)

Doctoral supervisors (Updated – 17/02/2021)

First Supervisor – Dr Monika A Formankiewicz (Anglia Vision Research)

Second Supervisor – Dr Sarah Lalor (Anglia Vision Research)

Third Supervisor – Dr Sarah J Waugh (External - University of Huddersfield)

Advisor - Dr Akash S Chima (External – University of the Highlands and Islands)

The research student and members of the research supervisory team are members of Anglia Vision Research, one of two research groups in the Department of Vision and Hearing Sciences, Faculty of Science and Technology. Quality Related (QR) funding (HEFCE) from the University is distributed to researchers via Research Group within the Faculties. Dr Monika Formankiewicz is the Director of Anglia Vision Research, a research group within the Department of Vision and Hearing Sciences, as well as the ARU Academic Lead for ACPOS (Addenbrooke's Community Paediatric Ophthalmology Service). ACPOS is the NHS Addenbrooke's Hospital funded service from which this project's participants will be recruited. It is hosted within the Department of Vision and Hearing's University Eye Clinic at Anglia Ruskin University.

Role of First Supervisor (The Research Supervisor): taken from "Expectations of First Supervisors" https://web.anglia.ac.uk/anet/rido/docschl/info.phtml

- To possess knowledge of key University contacts for research degree candidates and supervisors.
- To provide, with other members of the supervisory team, expert guidance and advice to the candidate.
- To respond promptly to all communications.
- To provide pastoral support for candidates.
- To communicate effectively with other members of the supervisory team.
- To be responsible for identifying other members of the supervisory team.
- To support the candidate in undertaking an initial assessment or revision of their Research Skills Training Needs Analysis.
- To ensure that research candidates undertake a programme of skills acquisition so that they can demonstrate a comprehensive range of research skills as determined by the Joint Statement of the Research Councils.
- To facilitate and monitor the research candidate's progress.
- To set objectives for the candidate to publish their research.

Role of the Research Student (The Principal Investigator): relevant aspects taken from "Research Degrees Regulations" for Anglia Ruskin University found at: https://web.anglia.ac.uk/anet/academic/research_regulations.phtml .

Training and Development: Research students are required by the RDSC to attend all of the compulsory sessions of the Researcher Development Programme. These are designed to support students during their programme of research and are part of the broader researcher development activity offered by the Doctoral School.

Stage 1 of the compulsory sessions is linked to the Research Proposal application. Stages 2a and 2b are linked to the application for Upgrade/Confirmation of Registration. Stage 3 is designed to help candidates prepare for their viva. As part of the Stage 1 training, all students must pass the online module *Intellectual Property in the Research Context*.

All candidates must complete a Research Skills Training Needs Analysis to establish their skills development needs and create a personal development plan. This must be updated and submitted each year as part of the process of Annual Review.

All postgraduate research degree candidates must attend either a) *Introduction to Research Ethics and Integrity (in Human Research)* development offered by the Doctoral School or b) pass the online module *Ethics 1 - Good Research Practice*. A copy of the relevant training certificate must be provided to the Researcher Development Programme Administrator in the Doctoral School.

All postgraduate research degree candidates whose research falls under risk categories yellow, red or purple (as determined by completing the Stage 1 Research Ethics Application Form), are also required to pass the online module *Ethics 2 - Research with Human Subjects in the Health and Social Sciences* or an equivalent course approved by the Chair of the appropriate Faculty Research Ethics Panel.

Intellectual Property
All postgraduate research degrees students are required to sign an undertaking that, in instances where they are formally notified as working on a project having commercial sponsors or commercial potential, they will enter into a confidentiality agreement, and assign their Intellectual Property rights to Anglia Ruskin.

Research Ethics: Research students need to consider ethical issues at an early stage and should consult the relevant web pages for further advice*:*

http://www.anglia.ac.uk/researchethics.

A Research Proposal Ethics Checklist must be submitted with the Research Proposal. Submission of the checklist does not constitute applying for ethical approval, which is a separate process. Approval from other entities (e.g. NHS, Ministry of Defence) is in some cases regarded as equivalent to our own. In cases such as the proposed study, HRA approval will be ratified by the Faculty of Science and Technology Research Ethics Panel (FREP).

Patient & Public Involvement

ARU encourages students and supervisors to identify and exploit opportunities for wider promotion of their research activities including media activities, public engagement, or

knowledge transfer activities where this might be desirable or appropriate and to demonstrate excellence and impact.

A previous study has been conducted by the Research Supervisor to obtain data using the same new visual acuity tests to be used in the proposed study, on 200 normal healthy children. A selection of these results have been accepted for presentation at Vision Sciences Society 2018, Florida, U.S.A. (Waugh, S. J. *et al.* (2018) 'Crowding distance in healthy children', in *Vision Sciences Society*). This initial study has allowed for previous public involvement to shape the design of the proposed research project.

The involvement of the public / patients in the proposed study will be participation during the testing / experimental phase.

Participants will be able to request access to the general conclusions of the study, and the results will be disseminated publically at research conferences and in scientific journals.

PROTOCOL CONTRIBUTORS

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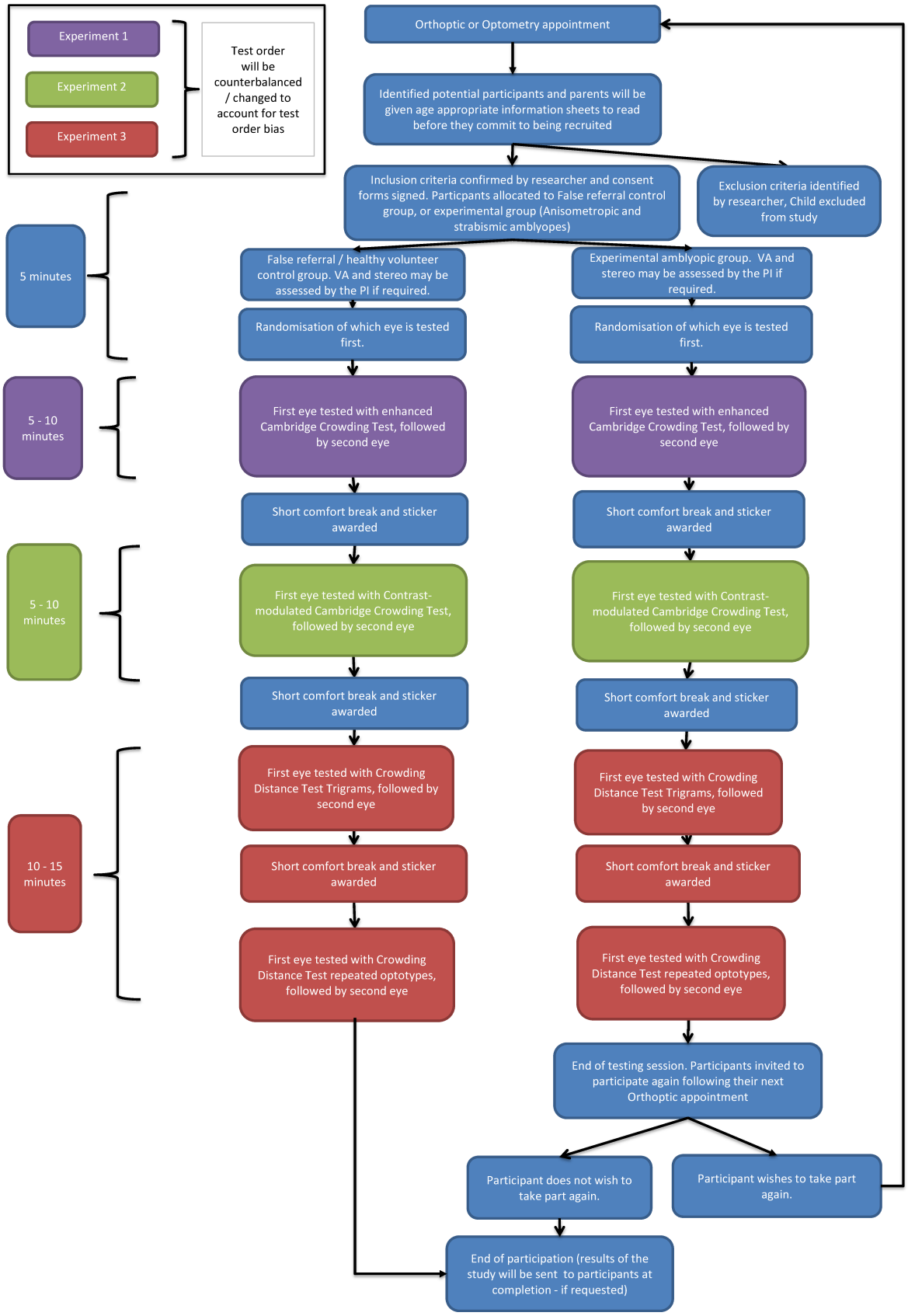
KEY WORDS: Amblyopia, visual acuity, crowding, anisometropia, strabismus, paediatrics.

PROPOSED STUDY FLOW CHART / GANTT CHART

Louisa Haine - PGR	Year 1 (2017-2018)				Year 2 (2018 - 2019)				Year 3 (2019 - 2020)			
	Oct - Dec	Jan - March	Apr - June	July - Sept	Oct - Dec	Jan - Mar	Apr - June	July - Sept	Oct - Dec	Jan - March	Apr - June	July - Sept
PHD RESEARCH ACTIVITY												
Research proposal writing and submission												
Literature Reading												
Protocol writing												
Ethical application writing												
Ethics board meeting (NRES)												
Experiment												
Data analysis												
Conference presentations												
THESIS												
Write up												
Title												
Literature review												
Methodology												
Results & data analysis												
Discussion												
Conclusions												
Abstract												
References and formatting												
Proof reading, Printing and Binding												
Submission of Thesis												Submit

STUDY FLOW CHART



Research protocol

Study title

An examination of new visual acuity and crowding distance tests, for better detection of amblyopia.

Short Study Title

New visual acuity and crowding tests for better detection of amblyopia.

Background:

Amblyopia, or 'lazy eye', is defined as a reduction in visual acuity (i.e. best corrected vision) of one or both eyes, due to abnormal visual development during childhood without organic cause (Von Noorden, 1974). Undetected and untreated it leads to permanent neurodevelopmental visual loss (Von Noorden, 1974; Daw, 2014). It is ordinarily associated with anisometropia (an interocular difference in refractive error), strabismus (ocular misalignment) or stimulus deprivation (such as seen in individuals with congenital cataracts). Amblyopia is thought to be due to the disruption of the normal development of binocular vision early in life (Wiesel and Hubel, 1963; Rauschecker and Singer, 1981; Crawford et al., 1983). It is a preventable and leading cause of monocular vision loss, with a prevalence of around 3% (Attebo et al., 1998), and increases the lifetime risk of bilateral visual impairment (BVI) from 10% seen in the general population, to 18% in amblyopic individuals (van Leeuwen et al., 2007). Early treatment of amblyopia is widely believed to be key to success (Epelbaum et al., 1993; Flynn et al., 1998, 1999; Wu and Hunter, 2006). Diagnosis of amblyopia is necessary for treatment to be initiated, therefore early diagnosis is important.

Amblyopia is a diagnosis by exclusion, with its principal diagnostic criterion being a reduction in visual acuity (Sengpiel, 2013). While visual acuity loss is the clinical diagnostic focus of amblyopia, amblyopia also affects other fundamental properties of spatial vision such as crowding, contrast sensitivity, hyperacuity, stereopsis and reading speed (McKee, Levi and Movshon, 2003; Hamm et al., 2014; Kelly et al., 2017; Birch and Kelly, 2017). Both strabismic and anisometropic amblyopia demonstrate reductions in visual acuity and contrast sensitivity, however strabismic amblyopes suffer additional spatial distortion of and abnormal spatial interactions between, visual targets. These quantifiable differences in spatial vision measured for the two conditions, indicate a difference in underlying neural bases for them (Hess and Bradley, 1980; Hess, Campbell and Zimmern, 1980; Levi and Klein, 1982; McKee, Levi and Movshon, 2003; Wong, 2012; Song, Levi and Pelli, 2014). More recently, evidence suggests that amblyopia not only affects visual processing at the primary visual cortex, but that the deficit due to amblyopia extends to, and becomes more exaggerated at, extra-striate cortex. For example, measures of modulation sensitivity for contrast-modulated gratings and detection of second-order motion show greater losses than are found for first-order stimuli (such as standard contrast sensitivity gratings) in the amblyopic eye (Wong, Levi and McGraw, 2001, 2005; Gao et al., 2015).

Amblyopia is particularly sensitive to the phenomenon known as “visual crowding” in which letters presented together are not as easily individually recognised as those presented in isolation (Korte, 1923). Despite numerous extensive medical and scientific studies, the process by which crowding causes visual confusion and impaired recognition of targets like letters, is still not fully understood (Levi, 2008). Initially, visual crowding was thought to occur

due to physiological and anatomical limitations of low-level cortical visual processing(Flom, Weymouth and Kahneman, 1963; Estes, Allmeyer and Reder, 1976; Ts'o and Gilbert, 1988; Gilbert et al., 1989), however more recent studies have demonstrated that higher cognitive factors such as figural and global aspects of visual processing, are strong contributors (Manassi, Sayim and Herzog, 2012; Herzog and Manassi, 2015).

Crowding is clearly demonstrated in peripheral vision in normal healthy individuals; middle letters of a word are harder to distinguish than letters on either end. However its presence has been confirmed in central vision of individuals with strabismic amblyopia, and to a lesser extent, those with anisometropic amblyopia (Stuart and Burian, 1962; Flom, Weymouth and Kahneman, 1963; Levi and Klein, 1985; Hess, Dakin and Kapoor, 2000; Kemper and Patel, 2011; Spiegel et al., 2013; Lev, Yehezkel and Polat, 2014)(Flom, Weymouth and Kahneman, 1963; Levi and Klein, 1985; Spiegel et al., 2013; Hess, Dakin and Kapoor, 2000; Kemper and Patel, 2011; Stuart and Burian, 1962; Lev, Yehezkel and Polat, 2014). This means that crowding can be incorporated into vision charts in a clinical setting, as its presence will enhance visual acuity loss in the central vision of amblyopic eyes, but not in normal eyes. Traditionally, high contrast visual acuity charts have been used to examine visual acuity limits. In amblyopia however, central vision can be much more restricted by crowding from visual clutter, than by visual acuity itself (Song, Levi and Pelli, 2014). Although currently available clinical vision charts attempt to incorporate crowding features, they are not successful at doing so in normal adults and some anomalous patients, and it is thought that they could be substantially improved (Hairol, Formankiewicz and Waugh, 2013; Formankiewicz and Waugh, 2013; Song, Levi and Pelli, 2014; Pelli et al., 2016). The proposed study will test whether

recent suggestions for theoretical improvements in vision tests will actually result in more favourable outcomes with respect to diagnosing amblyopia, in the target developing population, i.e., young children.

Rationale

In the UK, a national vision screening is employed to detect amblyopia and other undiagnosed visual conditions in school-aged children, so that they can be managed effectively. Better detection of amblyopia could be achieved by modifying current visual acuity tests, which measure the spatial resolution limit (or capacity for clarity and sharpness) of vision (Chung, Li and Levi, 2007; Formankiewicz and Waugh, 2013; Hairol, Formankiewicz and Waugh, 2013; Song, Levi and Pelli, 2014) and by measuring crowding distance; previously unmeasured in a clinical setting. By strengthening crowding magnitude, and better quantifying its spatial distance in paediatric populations, it is hoped that the ability to detect amblyopia, and monitor its improvement with treatment will be significantly enhanced.

Three recent suggestions regarding modifications to current visual acuity tests may lead to improved detection of crowding-sensitive conditions, such as amblyopia. First, closer placement of surrounding letters to the target letter should increase the magnitude of crowding in the amblyopic eye in particular, leading to increased visual acuity differences between eyes (Formankiewicz and Waugh, 2013; Lalor, Formankiewicz and Waugh, 2016). Second, contrast modulated stimuli should enhance crowding in amblyopic eyes (Chung, Li and Levi, 2007, 2008; Hairol, Formankiewicz and Waugh, 2013). Third, a new thinner font will allow clinical measures of foveal crowding distance (Pelli, Waugh, Martelli *et al.*, 2016). In this project, these three modifications will be tested for the first time in the target clinical population.

Formankiewicz and Waugh (2013) and Song, Levi & Pelli (2014) reported that optotypes (letters or symbols) on a vision chart should be placed closer together than they currently are on commercially-available charts, which use 2.5 to 5 stroke-widths separation between target and neighbouring letters. Closer placement disrupts target optotype identification in normal peripheral vision (Formankiewicz and Waugh, 2013) and in central vision of amblyopic eyes due to crowding (Song, Levi and Pelli, 2014). In one vision test in the proposed study, a laterally-reversible target letter (e.g., H, O, T or V) will be surrounded by four other letters (U, A, L, C). This arrangement, in which letters were separated by 0.5 optotype widths (or 2.5 stroke widths) was first formally used in the Cambridge Crowding Test (Atkinson *et al*, 1988). In the proposed experiments, the surrounding letters will be placed 1 stroke-width away from the target letter (see Figure 1), the optimal position recommended by recent studies (Formankiewicz and Waugh, 2013; Song, Levi and Pelli, 2014).

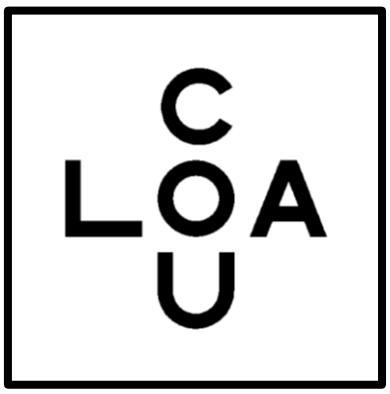


Figure 1: Modified Cambridge Crowding Test optotype arrangement

Visual acuities for target letters will be measured for both amblyopic and non-amblyopic eyes of child participants, in a clinical environment. These results will be compared with visual

acuities acquired during the clinical appointment using the Sonksen logMAR Test (SLT), which is the standard visual acuity test used in Cambridge University Hospital, Addenbrooke's Orthoptic Department (see Figure 2).

Figure 2: The Sonksen logMAR Test (SLT)

In the Sonksen logMAR Test (SLT), a single line of 4 letters separated from each other by 5 stroke-widths (or 1 optotype width), is contained within a box, separated from the letters also by 5 stroke-widths.

Recognition of target optotypes created by contrast-differences (second-order stimuli) is prone to greater crowding effects than is recognition of optotypes created by luminance-differences (first-order stimuli) (Wong, Levi and McGraw, 2001, 2005; Chung, Li and Levi, 2008; Hairol, Formankiewicz and Waugh, 2013). This effect is present in normal vision, however even greater visual losses for contrast-defined targets, as well as stronger crowding effects, have been reported in amblyopia (Chung, Li and Levi, 2008). By presenting a contrast-modulated (CM) target letter (H, O, T or V) surrounded by four other letters (U, A, L, C) placed 1 stroke-width away (in the modified Cambridge Crowding Test arrangement), this research aims to examine whether this second-order vision test will exaggerate differences between the eyes of amblyopic children, when compared to those measured in visually 'normal'

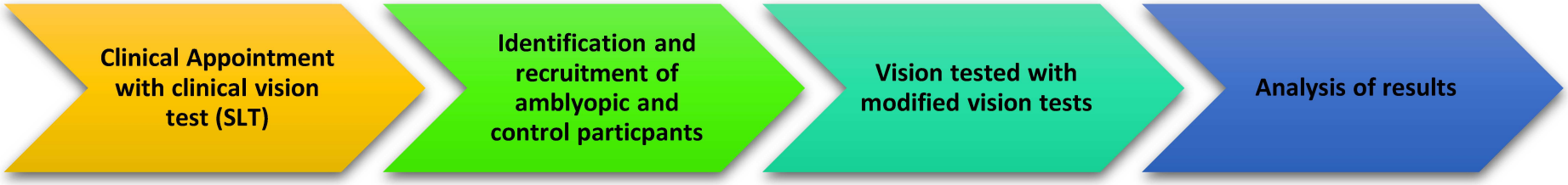
children. The results will again be compared to those obtained with the Sonksen logMAR test (SLT), a first-order vision test, to compare their sensitivities to amblyopia detection.

Finally, crowding distance, the spatial distance over which crowding occurs, in normal foveal (central) vision is small (2-4 arcmin) and cannot be measured with current standard clinical optotypes due to their large size (5 arcmin for 0.0 logMAR acuity) (Danilova and Bondarko, 2007; Huurneman et al., 2012; Siderov, Waugh and Bedell, 2013; Pelli et al., 2016). To get around this difficulty, a new vision test was recently created to quantify the crowding distance or "critical spacing" of crowding (Pelli, Waugh, Martelli *et al.*, 2016). It uses a new "Pelli" font (see Figure 3), which is much thinner horizontally than standard clinical fonts, allowing the optotypes to get closer to each other in physical space. This 'Crowding Distance Test' permits quantification of the critical spacing of crowding for the first time in a clinical population. The new "Pelli" font, each optotype appearing like tall skinny numbers, has already been trialled on 'visually normal' school-aged children (Waugh et al., 2018), but not yet examined on children with greater sensitivity to visual crowding, i.e., amblyopes. The third vision test in the proposed research, will investigate whether or not "crowding distance" measures made in each eye, results in greater inter-ocular differences, leading to better detection of anisometropic and strabismic amblyopia than does the current clinical standard visual acuity test, the Sonksen logMAR test (SLT).

Figure 3: 'Pelli' font

By using closer first-order target optotypes, second-order target optotypes, and quantifying crowding distance in paediatric populations, the ability to detect amblyopia and monitor amblyopia treatment, could be significantly improved for the first time since the 1960s. At that time crowding was first quantified in a clinical population of adult amblyopes (Flom, Weymouth and Kahneman, 1963) and was subsequently incorporated into commercially available tests as best practice.

THEORETICAL FRAMEWORK



Research questions and aims

Research question:

"Do the new vision test modifications offer better sensitivity to detection of inter-ocular difference leading to improved detection and monitoring of amblyopia, than the Sonksen logMAR test (SLT)?

Secondary research question:

"Is there a difference in sensitivities of these modifications to detecting strabismic amblyopia versus anisometropic amblyopia?"

Hypotheses

Null hypothesis 1 ($H1_O$): The new crowding tests do not offer better sensitivity to inter-ocular differences in acuity in amblyopic children, than the Sonksen logMAR test (SLT).

Alternative hypothesis 1 ($H1_a$): The new crowding tests do offer better sensitivity to inter-ocular differences in acuity in amblyopic children, than the Sonksen logMAR test (SLT).

Null hypothesis 2 ($H2_O$): There is no difference in the sensitivities of the new tests to detecting strabismic amblyopia, versus anisometropic amblyopia.

Alternative hypothesis 2 ($H2_a$): There is a difference in the sensitivities of the new tests to detecting strabismic amblyopia, versus anisometropic amblyopia.

The following steps will be taken in order to complete this project:

1. Critically appraise relevant literature about the effects of crowding on visual acuity in normal and amblyopic adults and children for first-order and second-order optotypes.
2. Design a study to incorporate three suggested modifications to current visual acuity and crowding tests, in a sample of child control and amblyopic participants.
3. Statistically analyse the results, comparing those obtained on control and amblyopic children, as well as with data already gathered from normal healthy children. Data from the new tests will be compared with each other and with those obtained using the standard clinical vision test (the Sonksen logMAR Test: SLT).
4. Accept or reject the given null hypotheses and discuss impact on clinical practice in a written thesis, as well as disseminate results at scientific conferences and in scientific peer-reviewed journals.

Study design, methods of data collection and data analysis

Study design

In this single centre study results from the 'Enhanced Cambridge Crowding Test', 'Contrast-modulated Cambridge Crowding Test' and the 'Crowding Distance Test' in their ability to detect amblyopia will be assessed using a prospective quantitative randomised controlled design. The results obtained from the experimental groups (anisometropic and strabismic amblyopia) will be compared to Sonksen logMAR test (SLT) results (assessed and documented by the ACPOS clinicians). They will also be compared to those obtained in this study from a control group. The testing will take place in a clinical room neighbouring the ACPOS (Addenbrooke's Community Paediatric Ophthalmology Service) clinic, which is hosted within the University Eye Clinic at Anglia Ruskin University (ARU).

Study procedure

Prospective participants will be identified by their clinician at their ACPOS clinical appointment, and given participant information leaflets. Healthy volunteers will also be accepted as control participants and given participant information leaflets. All participants will be required to provide informed assent, and their parent/guardian provide written informed consent before the experiments are conducted and after the nature and consequences of the study are explained. COVID tracking consent forms The recruitment and consent process will be monitored by the Principal investigator within the University Eye Clinic at ARU.

All tests will be conducted with the child's corrective lenses if required, after consent and assent is achieved. The child's Ophthalmology clinical team will be informed of their participation by use of an addendum into the clinical notes, if recruited through the ACPOS clinic. To reduce the risk of potential exposure to COVID-19 by participants during testing, the researcher will wear an apron and a mask. The researcher, participant and parent will wash their hands upon entering the testing room (which has its own sink and sanitising soap) and wear masks (Medical F2 as per ACPOS clinical protocol). Children under 11 may choose to not wear a mask. Individual risk assessments are conducted at the time of appointment creation by ACPOS/Addenbrooke's staff. All high-risk participants and parents will NOT have appointments entered into the recruitment system. All participants are children, so risk is minimal. All equipment will be Clinell wiped before and after use. Disposable occlusive patches and social distancing will also be used throughout testing.

The testing session is expected to take 45 to 60 minutes, depending upon the attention span and cooperation of the child; this includes regular breaks and relaxation points. It will not be possible to blind the researcher as to which group test participants have been allocated, as those patients with strabismic amblyopia will likely be easily identified due to the presence of their strabismus.

Background information will be recorded on data collection sheets (Appendix 1), and results of the vision tests are recorded as data files on the experimental/display computer. Participants need only complete one testing session, but may complete to 3 sessions over the

24 month period. Additional sessions would allow for analysis change over time. Participants are free to decide on the length of their participation and can leave the study at any time.

Background information

Prior to testing, the following relevant clinical information will be taken from the patient's digital medical records, or measured and recorded by the PI who is a registered Orthoptist;

1. Age
2. Gender
3. Diagnosis and Amblyopia subtype
4. Identification of fellow and amblyopic eye
5. Most recent SLT visual acuity result for each eye, for healthy volunteers this will be assessed by the PI.
6. Current refractive correction
7. Stereoacuity measurement. For healthy volunteers this will be assessed by the PI to ensure inclusion criteria are met.

This information will be used to identify which group the participant will be recruited to (anisometropic, strabismic or control) and also to aid randomisation of initial testing eye within each group. The participant will also be allocated a participant number and all results will be recorded using this participant number to preserve anonymity.

Randomisation

Each group will undergo covariate adaptive randomisation using minimisation to select which eye will be examined first (Hu et al., 2014). Test participants will have either their Amblyopic eye (AE) or Fellow eye (FE) assessed first for all 3 experiments, and control participants will have either their Right eye (RE) or Left eye (LE) assessed first. This will ensure equal distribution of known confounding variables (e.g. amblyopia density, occlusion regime, gender) for testing order bias between eyes. This minimisation process will allow for better statistical analysis and extrapolation of results. The order of experiments will be counterbalanced to prevent testing order bias.

It will not be possible to guarantee equal distribution within groups across age, as it is expected that most recruited participants will be around 5 years of age because the National Vision Screening programme occurs during the first year of school.

Materials

The presentation and control of visual stimuli will use custom-written Matlab programmes (MathWorks™, Natick, USA), using the 'Psychophysics Toolbox Version 3 (PTB-3)' on a 15"MacBook Pro with Retina Display, operating an Intel HD 630 Graphics card. The monitor will be calibrated and gamma corrected using an OptiCal photometer (Cambridge Research Systems). This will secure a linear progression of luminances, ensuring the input selected matches the luminance output produced, allowing for correct interpretation of the results. The screen resolution will be set to the highest possible spatial resolution (1920x1200 pixels)

and the frame rate will be set to the highest frame rate compatible with the aforementioned spatial resolution.

Optotypes for the 'Enhanced Cambridge Crowding Test', 'Contrast-modulated Cambridge Crowding Test' and the 'Crowding Distance Test' will each be printed onto respective matching cards, allowing for participants to point to what they see, if they are unable or unwilling to name the displayed visual stimuli.

Methodology

All participants will have the tests explained to them in the form of an astronaut story and they will complete tasks (the 3 modified vision tests) in order to help the astronaut complete his/her missions successfully. This will ensure that the examination is fun and engaging, with the aim of improving compliance and concentration. The eye not being tested will be occluded with an eye patch, or a patch that clings to a spectacle lens. All assessments will be completed at 3m, as this will allow the researcher to sit near the child so they can encourage compliance. Amblyopic eyes may be moved closer to the screen to accommodate for their poorer vision, and their threshold scores recalculated accordingly.

Staircase procedures will be used to measure vision (Lalor, 2018; Pelli, Waugh, Martelli *et al*, 2016; Waugh *et al.*, 2018). The staircase is a quick, efficient and popular method of determining an accurate visual acuity threshold; it is therefore an appropriate method of evaluating visual acuity thresholds with young children in clinical settings (Cornsweet, 1962; Corwin, Kintz and Beaty, 1979; Witton, Talcott and Henning, 2017).

Participants will be required to identify the central target optotype presented onto the screen, from different surrounding optotypes. No feedback will be given about the accuracy of their response. In each trial, unlimited time is provided for responses to be made, however prompt answers will be encouraged. Guesses are required when the target optotype is near to the participant's visual resolution limit. To mitigate anxiety for these trials, the staircase procedures also include intermittent "catch" trials, which are single large optotypes much larger (0.3 logMAR) than the expected acuity threshold. These catch trials do not contribute to threshold calculations. Catch trials also reduce the predictability of the test, another advantage when testing children (Bach, 1996).

A staircase procedure ends once visual threshold is reached. This involves averaging a number of reversals (normally 6), however the first 2 reversals are disregarded to prevent overestimation of the visual acuity threshold (Witton, Talcott and Henning, 2017). The total number of averaged reversals can be reduced from 4 to 2 if necessary with only a slight loss of accuracy, depending upon the child's age, concentration and attention span.

<u>Computer generation of visual stimuli</u>

In order to produce computer-generated visual acuity optotypes, every size of the two types of optotype (letters and 'Pelli' numbers) have been carefully checked and calibrated to ensure accurate physical size. Optotypes are constructed using Matlab (MathWorksTM, Natick, USA) matrices and scaled to allow for a large range of stimulus sizes to fit on the screen.

Psychophysics toolbox software (Pelli, 1997) is combined with Matlab for the generation and experimental display of sequences of stimuli. Optotype sizes produced and participant viewing distance (3m) is used to calculate an accurate size or logMAR acuity score (log of the minimum angle of resolution in minutes of arc). The custom-written program guarantees that all stimuli in this study are constructed in multiples of whole numbers of pixels, so that exact logMAR scores are calculated (not estimated). The lower limit of optotype size is restricted by a minimum number of pixels required to adequately form each optotype.

Contrast-modulated optotypes for the 'Contrast-modulated Cambridge Crowding Test' are created using dynamic noise (Smith and Ledgeway, 1997) to ensure that static luminance clumps are not useful for identifying them. Optotypes can then only be extracted by the visual system using differences in contrast, not luminance (see Figure 5). For each stimulus frame, different binary (black or white) checks of noise are drawn onto the screen and the noise is multiplied by a square-wave optotype profile. The screen cycles through several noise pages every 4 temporal frames (tied to the temporal resolution limit of the screen), so that the noise appears to twinkle in time. The size of the black and white noise checks on the stimulus screen is scaled to the overall optotype size, such that each letter consists of 15 noise checks, which has been found to be most effective for measurement of vision (Pelli and Farell, 1999) and ensures that the noise is resolvable at all optotype sizes.

<u>Experiment 1 –Enhanced Cambridge Crowding Test</u>

The participant will be shown the Cambridge Crowding Test letter matching card prior to the start of the experiment, and asked to name the letters, with whatever names they wish to

use. If they cannot do this with ease, they will be allowed to match what they see, by pointing to an optotype on the matching card (see Figure 4).

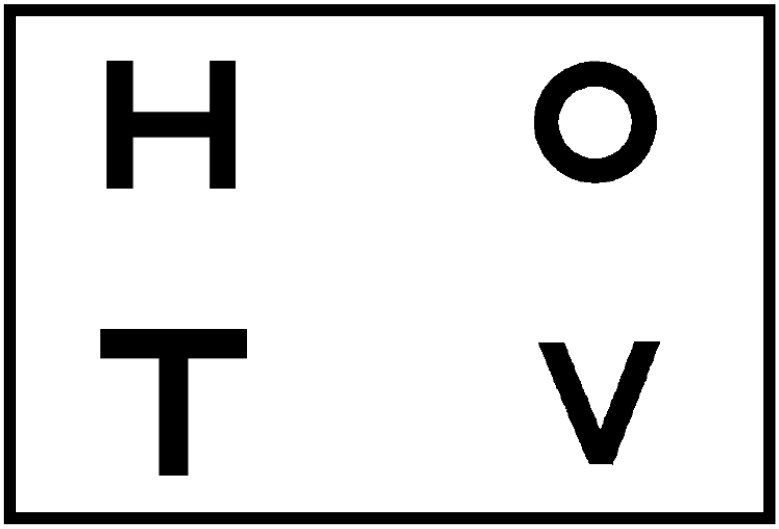


Figure 4: "Enhanced Cambridge Crowding test" matching card

A laterally-reversible target letter (e.g., H, O, T or V) will be displayed and surrounded by four other letters (U, A, L, C) as per the Cambridge Crowding Test (Atkinson et al., 1988). The surrounding letters will be placed 1 stroke-width away from the target letter (see Figure 1). Isolated letters will also be presented. The child will identify the central letter only. Once threshold is reached the experiment will stop. After a short break, the second eye is tested in the same manner. It is expected that this should take approximately 5 minutes based on pilot experiments. This is the end of experiment 1.

Experiment 2 – Contrast-modulated Cambridge Crowding Test

The participant will again be allowed to match (see Figure 5) or name the visually displayed optotypes.

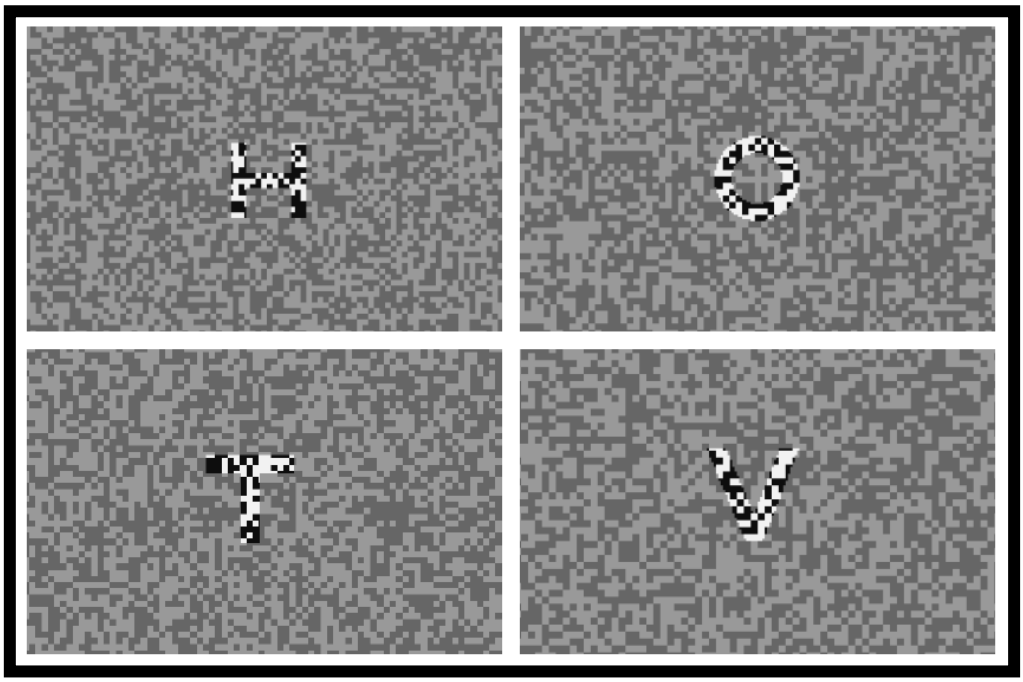


Figure 5: "Contrast Modulated Cambridge Crowding Test" matching card

A contrast modulated letter will be displayed on the computer screen in an arrangement as per Experiment 1, with the surrounding letters placed 1 stroke-width away from the target letter. The participant will identify the central letter, the size of which will vary according to the staircase procedure until size threshold is reached; then the experiment will stop. Examination of both eyes will take approximately 5 minutes, including a comfort break, based on pilot experiments.

Experiment 3 – "Crowding Distance Test"

The participant will be shown the "Crowding Distance Test" matching card prior to the start of the experiment, and ask to name the numbers. They will be able to indicate what they see by either calling out the number or pointing to it on the matching card (see Figure 6).

Figure 6: "Crowding Distance Test" matching card

A trigram arrangement (a trio of numbers) with 1 stroke width separation, will be presented according to an adaptive staircase procedure. The child will identify the central number and visual threshold will be established using a staircase procedure. The second eye will be examined in the same manner taking approximately 5 minutes, based on pilot experiments.

Following a short break, repeated numbers (two repeating numbers that fill the screen) separated by 1 stroke width separation, will be presented. The repeated arrangement is helpful when eye movements are unstable, as it allows the eye to find the target optotype regardless of where on the screen it lands. This procedure will be repeated with the other

eye. The anticipated time to complete the measure in both eyes is around 5 minutes. This is the end of Experiment 3, and the end of the testing session.

The order of tests or experiments will not always be the same, but will be counterbalanced across participants within any experimental group to ensure that thresholds are not biased due to practice, attention, or fatigue effects.

Throughout the study, participants will be offered stickers and stamps on a 'passport' to maintain interest and concentration, as well as making the study fun and engaging. The tests follow a story line about a teddy astronaut visiting outer space, and alien toys helping the participants to interpret the signs (optotypes) along the way. Soft toy teddies and aliens will decorate the room and be available to help the child if need be. This has been found to be helpful particularly with young children (Waugh *et al*, 2018).

Following completion of the vision tests, participants will be asked if they wish to be involved again with the study. If they do, then they will be tested again following their next Orthoptic review with the ACPOS clinic, or at a time that suits the family best. If they do not, this is the end of their participation.

<u>Consideration of measurement tools, validity and reliability</u>

The results will be generalizable to the entire UK screening population of 3 to 11-year-olds, due to the use of a control group, ensuring external validity.

Participant bias will be controlled and intra-observer reliability maximised using the rigorous set of forced-choice psychophysical testing procedures described above and a single specialized researcher. The researcher is a qualified clinical Orthoptist with many year's experience working with children in vision screening clinics, ensuring that the results will be obtained as accurately and consistently as possible. Test/re-test reliability is ensured by the use of randomization of the order in which the eyes are examined, and counterbalancing the order of the experiments.

Statistical consideration and Data management and analysis

Anonymised data from the 3 experiments will be stored digitally on the experimental computer, which is password protected and only accessible to members of the research team. Data will be compiled in an Excel spreadsheet, ready for analysis.

The data will be analysed using SPSS or Statistica with Repeated Measures Analysis of Variance models. Visual acuities, crowding and critical spacing estimates will be compared between normal and amblyopic groups. Confirmation of normality and sphericity will be assessed with a Shapiro-Wilk test and Mauchley's Test of Sphericity and where necessary, error rates will be adjusted with a Huynd-Feldt Correction in order to ensure that type 1 errors (incorrect rejection of the null hypothesis) are less likely.

The rate of improvement of visual acuity, crowding and critical spacing over the treatment period will also be compared (in those participants who opt to complete more than one assessment session) between the three modified tests, and the SLT.

A Bland-Altmann analysis will also be used to assess levels of agreement between the different test measures, rather than examination of correlation alone. This is because while a high correlation may be an interesting finding, it does not necessarily indicate agreement between the different test measures (Martin Bland and Altman, 1986).

Study Setting

The study will take place in a first floor clinical room with daylight fluorescent lighting, within the University Eye Clinic on Bradmore Street, Cambridge; and will take place Monday to Friday, 9am to 5pm.

Clinic Address:

University Eye Clinic,

Bradmore Street,

Cambridge,

CB1 1PT

Telephone:

01223 698070

Site	Activities
ACPOS clinic - based at the University Eye Clinic	**Patient Identification point** Potential participants approached and given study information leaflets by ACPOS clinician.
Experimental/clinical room – based at the University Eye Clinic	Recruitment, consent, recording of background information, completion of visual acuity testing.

The study room is a modified clinical room. It contains appropriate seating for a participant to be tested as well as sufficient and comfortable space for the presence of the researcher and the participant's parent/guardian. Bathrooms are located on the same corridor, and access to the first floor is available via stairs or a lift. Telephones are present within the testing

room and additional staff are present in the building at all times the clinic is open, ensuring that help can be obtained at all times should an unexpected emergency arise. University first-aid is available directly using the phone in the testing room. The clinical suitability of these rooms for the purposes of visual acuity assessment has been evaluated by Anglia Ruskin University and an appropriate risk assessment has been completed.

Sample and Recruitment

Study population and sampling technique:

This study will prospectively examine children who fail vision screenings at school and those already being treated. Amblyopic and control participants (aged 3 to 11 years) will be identified via ACPOS (Addenbrooke's Community Paediatric Ophthalmology Service) hosted by the University Eye Clinic. The ACPOS clinic will be a Patient Identification Centre (PIC), and an information poster will be present in the ACPOS waiting room to alert patients that they may be asked if they would like to participate (Appendix 1).

Potential participants will have been identified by ACPOS clinicians as having anisometropic or strabismic amblyopia. Control participants of similar age will also be recruited via the ACPOS clinic as false positive referrals from the screening service. Healthy volunteers will also be acceptable as control participants. The pool of amblyopes projected for 18 months is *n*=278; 60% strabismic, *n*=167 (based on a 2016-2017 Addenbrookes audit).

As the participants will mostly have undertaken the normal screening programme and be following treatment plans as guided by the Royal College of Ophthalmology, these results should be able to be generalised to all UK 3 to 11-year-olds diagnosed with amblyopia.

Eligibility Criteria – Inclusion criteria:

- **Test participants;** Male and female 3 to 11-year-old children diagnosed by ACPOS clinicians as likely having amblyopia (strabismic or anisometropic). They will be tested following 6 weeks (or more) of refractive adaption.

- **Control Participants;** Male and female 3 to 11-year-old children who have been falsely referred into the Hospital Eye Service (ACPOS) by the visual screening service, or healthy volunteers who have satisfactory visual functions, as per the national screening guidelines.

- **All participants** must be able to complete the Sonsken logMAR Test (SLT) either verbally or via use of a matching card.

Eligibility Criteria – Exclusion criteria:

- Uncorrected refractive error.
- The presence of any other vision limiting medical condition, not listed in the inclusion criteria.
- Any prior or existing medical history of epilepsy or seizures.

Sample Size:

Based on data produced from previous studies, the outcome data obtained from this study will come from an underlying continuous and normal distribution.

As the first alternative hypothesis is two-tailed, a t-test is appropriate for the calculation of sample size, to find an estimated effect size, with standard deviations known for the visual acuity measures (Hulley and Cummings, 1988). A comparison of means during statistical analysis (Repeated Measures ANOVA) makes this a suitable strategy for determining sample size.

The effect size is set at 0.100 logMAR, which is the minimum inter-ocular difference that should exist for the participant to be classified as amblyopic (Elliott and Firth, 2009). The standard deviation of the visual acuity measure is set as ±0.100 logMAR. In adults, visual acuity repeatability measures of ±0.1 logMAR have been found (Klein et al, 1983; Arditii & Cagenello, 1993; Siderov & Tiu, 1999). Lalor (2018), who used staircase procedures like those proposed, found for children aged 3 to 16 years, standard deviations of ±0.06 logMAR. Pilot studies with the Crowding Distance Test have suggested even lower standard deviations of the test measures (Waugh et al., 2018).

Using a standardarised effect size of 1 (effect size/sd of measure; or Cohen's *d* of 1), a significance level or probability of committing a type 1 error (incorrect rejection of null hypothesis), of 0.05; and the probability of committing a type 2 error (incorrect acceptance of null hypothesis) of 0.2 (power of 0.8), a sample size of *n*=16 participants in each group

(amblyopes and control participants) will be required to achieve statistical significance, if a difference exists.

In brief, the data generated will be analysed using a Repeated Measures Analysis of Variance (with Huyndh-Feldt correction for violation of sphericity of variance). In this procedure means are compared. Also post-hoc Tukey comparisons between groups can be made; or a Dunnett test comparing each group (anisometropic; strabismic) to the control group (normal controls)

The above calculation is sufficient for a comparison of means. The second hypothesis involves three distinct groups with independence of observation. An alternative way to estimate sample size is to conduct a one-way ANOVA using an effect size *Cohen's f*, is set at 0.4 (for "large" effect size) to examine for large effect sizes. Once again, the significance level or probability of committing a type 1 error is set at 0.05, and the probability of committing a type 2 error is set at 0.2, to yield a study power of 80%.

Following this power calculation, a sample size of *n=21* participants in each group (anisometropic amblyopes, strabismic amblyopes and control participants) will be required to achieve statistical significance, if a difference exists.

These figures produce an estimated total sample size of *n=32* for testing Hypothesis 1 (16 amblyopes and 16 controls), and *n=63* for testing Hypothesis 2 (21 anisometropic amblyopes, 21 strabismic amblyopes and 21 controls).

In order to fulfil both these criteria for hypotheses 1 and 2, and achieve statistical significance, we will recruit *n=21* in each group (anisometropic amblyopes, strabismic amblyopes and control participants), with a total recruitment number *n=63.*

Recruitment and identification of participants:

The study will be publicised in a number of ways.

1. A poster will be displayed in the waiting room of the ACPOS clinic in order to raise awareness of the study to those who attend the clinic (Appendix 1).
2. Clinicians / the direct care team at ACPOS, will identify eligible participants during their clinical appointments, and offer them a study information leaflet. ACPOS will be the Patient Identification Point (PIC). An application will be made for the Principal Investigator to have a research passport (letter of access/ honorary research contract) in order to help identify potentially suitable participants attending the ACPOS clinic. The Principal Investigator is suitable for this task as she worked as the clinician in this clinic prior to starting this study.

Interested persons will be given the parent / guardian and paediatric information sheets (Appendix 1) and their medical history checked to ensure they meet all the inclusion criteria and none of the exclusion criteria, prior to recruitment. For ACPOS individuals who do not wish to take part, the clinician will add an addendum to the participant's clinical notes to ensure that the participant is not approached again as a potential participant.

The clinician will notify the researcher if the participant wishes to take part, or the participant can contact the researcher directly using the details on the information leaflet. The researcher will then discuss the research with the prospective participant and their parent/guardian, giving opportunity for further questions to be asked and answered. If the participant and their parent/guardian demonstrate understanding of the requirements of the study and wish to consent to take part, the parent/guardian will be given a consent form to sign, and a record of clear assent will be taken from the participant (Appendix 1). Both parental consent and clear participant assent must be obtained in order for the participant to be recruited. Once consent and assent are provided, the researcher will add an addendum to the participant's clinical notes to inform clinicians. This will again ensure that the participant is not repeatedly approached as a potential participant.

While participants will not be paid for their participation in the study, they will be offered a £10 Amazon gift voucher as compensation for their time as a result of participating in the study.

Ethical considerations

This research will be conducted in full conformation with the principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of the United Kingdom; and on approval by Anglia Ruskin University and the local NHS research ethics committee (REC). Prior to recruitment, participants will be given full written information about the study, in order to allow them to make an informed decision as to whether or not they wish to participate. Participation will require both signed informed consent from a legal guardian and informed assent from the child following the provision of age appropriate written information. Participants can also withdraw from the study at any point without any given reason, without prejudice.

The sensitivity of the new tests, compared with the existing SLT test, will not be known until data analysis is complete. If the data suggest that the new tests provide additional useful clinical insight into the participant's visual condition, this information will be shared with the Ophthalmology clinical team to ensure the participants continue to receive appropriate management.

The supervisory team already hold ethics approval to conduct similar testing on children who attend the University Eye Clinic outside the hospital system, and the researcher is a trained Orthoptist with many years of clinical hospital experience, testing vision in children and adults.

Assessment and management of potential risks:

Possible potential for Physical harm: Eye strain and fatigue. Screen refresh rates and flicker present in contrast-modulated optotypes may be a trigger for individuals with a history of seizures or Epilepsy, therefore individuals with these conditions are excluded from this research.

Potential for distress: Subjects may become slightly anxious or bored, if they struggle to visually identify images when asked. Mediation of anxiety and boredom can be managed providing support and encouragement throughout testing, by delivering the testing in the form of a game thereby making testing fun, and ensuring that the subject knows they can withdraw from the testing at any time. Boredom will also be reduced by use of Catch trials, in order to ensure that the child has not become disengaged with testing.

Participants and parents/guardians will be informed of these risks prior to recruitment in written form. Children will also be given age appropriate written information explaining what they will be doing. This will also be explained again verbally, prior to consent forms being signed.

Patient safety

The following precautions have been taken for this study,

- Any child with a prior or existing medical history of epilepsy or seizures will be excluded from the study, due to an associated risk of screen flicker.
- Each examination will take place in a well-lit testing room at Anglia Ruskin University, with the child's parent / guardian present at all times during the experiment.
- Regular breaks will be given throughout testing in order to prevent fatigue and boredom.
- Participants are free to withdraw from the study at any point without any given reason and without prejudice.
- If the participant reveals information which raises safeguarding issues, then these concerns will be raised with the child's clinician, who will be able to check if the child already has protection plans in place and ensure that the hospital or community safeguarding team can examine the situation in more detail.

There are minimal risks to the child participants. These are similar to those experienced during normal clinical appointments. Frequent breaks between tests are always possible and they are made to be fun and engaging. Sometimes the child will need to guess, but support and encouragement will be provided throughout.

Research Ethics Committee (REC) and other reviews

Peer Review

This study proposal has been examined by the Research Supervisory Team prior to submission to the FRDSC (Faculty Research Degree Subcommittee) for peer review.

This proposed study has been approved by three reviewers, two with subject-specific expertise, from outside the Research Supervisory Team, but within the Faculty of Science and Technology, Anglia Ruskin University. The report by reviewers recommended (on 21/2/18) that the research proposal is approved by FRDSC, as being suitable for PhD level study. Approval will be ratified at the FRDSC meeting 3/5/18.

Research Ethics Subcommittee (RESC)

This Subcommittee of the Research Committee considers policies and procedures relating to the ethics of research investigations involving human participants, human tissue and organs, animals and other research that presents ethical issues undertaken by staff and students of Anglia Ruskin University. Responsibility for the approval of individual research ethics applications is devolved by Research Ethics Subcommittee to Faculty Research Ethics Panels. Before the start of the study, a favourable opinion will be sought from the HRA and a REC for the study protocol, informed consent forms and other relevant documents.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site and all correspondence with the REC will be retained.

It is the Chief Investigator's responsibility to produce the annual reports as required and the Chief Investigator will notify the REC of the end of the study. An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended.

If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

The Chief Investigator will ensure that appropriate approvals and research passports/letters of access from participating organisations are in place before any research takes place.

Amendments

For any amendment to the study, the Chief Investigator, in agreement with the sponsor will submit information to the REC in order for them to issue approval for the amendment. The Chief Investigator will work with sites (Addenbrookes R&D, the ACPOS clinic and ARU) so they

can put the necessary arrangements in place to implement the amendment to confirm their support for the study as the amendments state.

Patient & Public Involvement

ARU encourages students and supervisors to identify and exploit opportunities for wider promotion of their research activities including media activities, public engagement, or knowledge transfer activities where this might be desirable or appropriate and to demonstrate excellence and impact.

A previous study has been conducted by the Research Supervisor to obtain data using the same new visual acuity tests to be used in the proposed study, on 200 normal healthy children. A selection of these results have been accepted for presentation at Vision Sciences Society 2018, Florida, U.S.A. (Waugh, S. J. *et al.* (2018) 'Crowding distance in healthy children', in *Vision Sciences Society*). This initial study has allowed for previous public involvement to shape the design of the proposed research project.

The involvement of the public / patients in the proposed study will be participation during the testing / experimental phase.

Participants will be able to request access to the general conclusions of the study, and the results will be disseminated publically at research conferences and in scientific journals.

Protocol compliance

The Chief Investigator will be expected to conduct the study in compliance with the approved protocol agreed upon by the Sponsor and REC approval. All protocol deviations should be identified, documented and reviewed for impact on subject safety and data integrity by the Chief Investigator. The Chief Investigator should implement any required operational corrective action to address deviations and collaborate with the Sponsor/ research supervisory team to determine whether a deviation requires a protocol amendment.

Data protection, storage and destruction policy:

As per the university and UK Data service guidelines, data generated by and pertaining to this study will be appropriately destroyed at the following intervals;

Pseudo-anonymised research data based on clinical samples for public health	To be kept (in encrypted form) for between 15 – 20 years and then destroyed.
Consent forms	To be securely kept at the University with the research data as per the UK Data service guidelines.

Hard copies of personal data (consent forms and anonymised data sheets) will be stored throughout the duration of the study in a locked filing cabinet within the Department of Vision and Hearing Sciences, Anglia Ruskin University; in a secure room requiring passcode protected access. Digital copies (all password protected) of the study information (pseudo-anonymised

with name removed), will be scanned and encrypted and stored on University password-protected virtual space accessible only to members of the research team, after which physical copies will be confidentially shredded at the conclusion of the study. Data will be shared publicly via University protected space known as ARRO (ARU Research Repository Online) https:\\arro.anglia.ac.uk. The data will also become open-access if required during the publication process. This research is not externally funded, however the data will be stored for 20 years after publication on the University secure space, according to RCUK Concordat on Open Research Data.

It will be the responsibility of the Principal investigator to ensure that the filing cabinet holding personal data during the term of the project is not accessed by any person outside members of the research team. She will also ensure that after the retention period, these paper-based data are confidentially shredded using University systems for doing so.

Confidentiality

In accordance with General Data Protection Regulation (GDPR), the following precautions will be taken;

- The results will be obtained and processed for a specific purpose, with full-informed assent given by the subject and informed written consent by their guardian.
- The information gathered will be relevant and not excessive for the purpose of the study.

- The information gathered will not be kept for longer than necessary.
- The personal patient information will be kept in a locked secure filing cabinet, and all the results anonymised.
- All digital information will be anonymised and password protected. The data cannot be overwritten and is backed-up to a secure, university owned, password protected wireless hard drive.

Indemnity

Indemnity will be provided by Anglia Ruskin University who have hold professional indemnity insurance with U.M Association Limited (Appendix 1).

Professional Indemnity details

Limit of Indemnity	£10,000,000 any one claim and in the aggregate except for Pollution where cover is limited to £1,000,000 in the aggregate.
Cover provided by	U.M. Association Limited and Excess Cover Providers led by CNA Insurance Company Limited

Clinical Trials liability details

Limit Of Indemnity	£30,000,000 any one claim and in the aggregate, including claims costs and expenses.
Cover provided by	U.M. Association Limited and Excess Cover Providers led by QBE Insurance (Europe) Limited

Public and products liability details

Limit Of Indemnity	£50,000,000 any one event and in the aggregate in respect of Products Liability and unlimited in the aggregate in respect of Public Liability.
Cover provided by	U.M. Association Limited and Excess Cover Providers led by QBE Insurance (Europe) Limited

Employers' liability details

Limit of Indemnity	£50,000,000 any one event unlimited in the aggregate.
Includes	Indemnity to Principals
Cover provided by	QBE Insurance (Europe) Limited and Excess Insurers.

Access to full dataset

Only the Chief investigator, Principal investigator and the allocated Research Supervisors will have access to the full dataset for this single centre study. It is not envisaged that the dataset will be used for secondary analysis. Site investigators will be granted access to the full dataset, only if a formal written request is made to the FRDSC, and approved.

Study Outcome Dissemination

Exploitation and Intellectual Property Rights

ARU asserts the right to ownership of all intellectual property (IP) rights arising from research it funds through a VC PhD Studentship. A student should not enter into any agreement that may affect rights to exploit the IP arising from their work without first consulting the Director of RIDO (Research and Innovation Development Office of ARU).

Publication and Dissemination of Research

On completion of the study, the data will be analysed and tabulated and a Final Study Report prepared. It is ARU policy that the results of the research it supports should be disseminated as widely as possible, for the benefit of other researchers and of the wider community.

ARU has established arrangements for ensuring that the results and full anonymised dataset are deposited in an on-line repository and made available to other researchers. Researchers should consult their supervisors about those arrangements, as to which on-line repository would be most suitable for their research area. In this study, data will be stored via the internal publications repository known as ARRO. Doctoral students should ensure that their thesis (or any other output such as an exhibition or performance) includes an acknowledgement of the support they have received from ARU.

Publication of any aspect of the research resulting from an ARU-funded studentship, through publications and other forms of media communication, including media appearances, press releases and conferences, must acknowledge the support received from the ARU.

Research students should discuss with their supervisors whether any or all of the results of their work should be published. If a student, or anybody else, publishes any aspect of the research resulting from an ARU funded studentship, through publications and other forms of printed or electronic media communication, including media appearances, websites, press releases and conferences, they must acknowledge the support received from ARU.

Learned societies and other organisations (such as the Institute of Historical Research) collect and publish information about doctoral theses completed and in progress. ARU strongly urges the submission of relevant information if asked to do so.

It is anticipated that this study will be written in an appropriate journal style, authored by the Principal investigator and the student research supervisors, and published in a leading vision science or medical journal such as *Journal of Vision*, *Vision Research, British Journal of Ophthalmology, Investigative Ophthalmology and Vision Science* or *Nature*. Results will also be presented at appropriate scientific and medical conferences such as *the Vision Sciences Society (VSS)* and *the Association for Research in Vision and Ophthalmology (ARVO).* The outcomes and results of this research will be made available to all of the participants of the study in a written format using suitable and understandable lay language. It will also be possible for the participant to specifically request results after the results have been published.

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Appendices

Appendix 1 – Documentation

CURRICULUM VITAE

Name:	
Mrs Louisa Haine	
Present appointment: *(Job title, department, and organisation.)*	
Post Graduate Researcher, Anglia Vision Research, Anglia Ruskin University, Cambridge.	
Address: *(Full work address.)*	
Louisa Haine, Anglia Vision Research, Department of Vision and Hearing Sciences, Room 407, Coslett Building, Anglia Ruskin University, Cambridge.	
Telephone number:	**Email address:**
(01223) 698584	louisa.haine@pgr.anglia.ac.uk
Qualifications:	
BSc (Hons) Orthoptics City and Guilds PTLLS City and Guilds CTLLS MMedSci (Vision and Strabismus)	
Professional registration: *(Name of body, registration number and date of registration.)*	
HPC – reg no. OR 05763, registered since 01/09/2009 BIOS – reg no. 3121 since 01/01/2010 Society for Education and Training, associate status – member no. **AH000082,** registered since 09/04/2013	

Previous and other appointments: *(Include previous appointments in the last 5 years and other current appointments.)*

01/04/17 – 10/11/17: Specialist Orthoptist, Addenbrookes Hospital, Cambridge.

01/07/11 – 01/04/17: Lead Orthoptic Clinical Tutor, Addenbrookes Hospital, Cambridge.

01/09/08 – 01/07/11: Orthoptist, Addenbrookes Hospital, Cambridge.

Research experience: *(Summary of research experience, including the extent of your involvement. Refer to any specific clinical or research experience relevant to the current application.)*

Taken part in departmental audits including completing questionnaires, obtaining patient notes for audit purposes, written a paper on superior oblique myokymia and obtained patient consent to use their details for a published case study.

Completed a research project as part of the MMedSci. This involved writing of research protocols and information leaflets, obtaining local NHS ethics approval using the IRAS system, recruitment of participants, randomisation, assessment and statistical analysis.

Obtained monies via a grant application to the Cambridge Eye Trust, to help fund the purchase of equipment necessary for the vision and strabismus MMedSci research project.

Research training: *(Details of any relevant training in the design or conduct of research, for example in the Clinical Trials Regulations, Good Clinical Practice, consent or other training appropriate to non-clinical research. Give the date of the training.)*

GCP certificate: 16/8/2016

Epigeum online – Intellectual property in the research context: 03/10/2017

Epigeum online - Ethics 1: Good Research Practice: 02/10/2017

Relevant publications: *(Give references to all publications in the last two years plus other publications relevant to the current application.)*

August 2014: Poster presentation at the British and Irish Orthoptic Society Scientific Conference - Glasgow: **'A CASE OF CHRONIC SUPERIOR OBLIQUE MYOKYMIA WITH COMPENSATORY HEAD POSTURE'.**

Signature:	**Date:**
L.Haine	26/3/18

Cambridge University Hospitals NHS
NHS Foundation Trust

a.r.u.a.r.u. Anglia Ruskin University

INFORMATION FOR PARENTS / GUARDIANS

ARU's response to COVID -19 pandemic.

ARU takes its responsibilities regarding COVID-19 seriously. Further details regarding this are provided below.

Test and trace

As part of ARU's response to the COVID-19 pandemic, we need to collect personal data from you, in order to support the Government's 'test and trace' system. For further information, please refer to ARU's Privacy Information for COVID-19 Management at: https://aru.ac.uk/privacy-and-cookies/research-participants

We will ask you to sign a consent form to confirm that you are happy for us to collect this information. Further information is provided on this consent form. Please let me know if you have any queries regarding this.

Health & Safety

It is not advisable for people in the clinically vulnerable or clinical extremely vulnerable (shielded) categories to take part in any face to face research.

It is an ARU requirement that a Risk Assessment (Health and Safety) is carried out for all face to face research. Please refer to ARU's website at https://aru.ac.uk/coronavirus/Covid-secure-campuses for information about what ARU is doing to manage the risk of Covid-19.

During this study, the researcher will wear an apron and a mask. The researcher, participant and parent will wash their hands upon entering the testing room (which has its own sink and sanitising soap) and wear masks. Children under 11 may choose to not wear a mask. Where disposable equipment cannot be used, all equipment will be cleaned before and after used. Social distancing will also be used throughout testing.

Title of Project: New visual acuity and crowding tests for better detection of amblyopia.

Secondary title: Examining new vision tests for better detection of childhood visual loss.

IRAS project ID number: 238449

We would like to invite your child to take part in our research study. Before you as a parent / guardian decide, we would like you to understand why the research is being done and what it would involve for you and your child.

One of our team will go through the information sheet with you and answer any questions you have.

Please talk to others about the study if you wish, and decide whether or not you and your child would like to take part. Ask us if there is anything that is not clear.

What is the purpose of the study?

This study aims to investigate whether new changes to vision tests will offer better sensitivity for detecting amblyopia (or "lazy eye") compared to what is currently used.

Your child has been invited to participate because they have been diagnosed with amblyopia or have no visual concerns, and they are the right age for this study.

Who is doing the research?

This research is being conducted by Mrs Louisa Haine under the supervision of Dr Sarah J Waugh within the discipline of Vision and Hearing Sciences at Anglia Ruskin University. Mrs Haine is a qualified orthoptist and Dr Sarah Waugh is a consultant optometrist.

Does my child have to take part?

No, it is entirely up to your child and you, whether or not you decide to participate. If you do decide to take part, both you and your child will be given time to discuss the study with a research member of staff and to ask any questions. As a parent / guardian, you will be asked to provide written consent, and your child will be asked if they want to participate, before we commence with the research project.

What if myself or my child change our minds?

Your child can withdraw from the study at any time, without having to give a reason. There are no negative consequences to yourself or your child should you wish to withdraw. Any data already collected will be retained by the researchers, however it will be anonymised so that no-one would be able to identify information about any particular individual.

What do we have to do?

You and your child would be required to visit the Anglia Ruskin University Eye Clinic, ideally following their routine NHS eye exam, if required, to participate in the research. The research only requires one single visit. It would be valuable to us if we could repeat the research after additional routine future follow up clinical appointments, if required, however this is completely optional, and identical to the first visit. If your child does not attend the hospital eye clinic, your child will have their vision and 3D vision measured by a qualified orthoptist prior to commencing the research.

During the research session, your child will participate in a number of computer generated vision tests. They will be asked to identify the letters / numbers either verbally or by matching what they see on a card. Each eye will be tested. The tests are designed to be engaging and fun, and we use stickers, stamps and praise to encourage your child.

The results of these computer vision tests will be compared to the results of the vision test that your child performed during their routine clinical eye appointment. We ask that you consent to us as researchers to ask your child's clinician about these, and access their clinic notes. If during research any 'incidental findings' are found with these new 'un-validated' tests, then

these will be reported to your child's medical team (with your consent) who can re-examine your child's clinically validated results where needed. Please ask the researcher if you would like further clarification regarding this.

What are the possible disadvantages and risks / side effects of taking part?

Please advise the researcher if you are concerned that you or your child are at high (clinically vulnerable) or very high risk (clinically extremely vulnerable) of contracting COVID-19, so that we can consider excluding you from this research study. If you have appointments in ACPOS this is unlikely, but we are happy to discuss this with you. We take the same precautions to minimise risks for all of our research participants as are taken in ACPOS.

The examination would require you and your child to remain at the Anglia Ruskin University Eye Clinic, for 30 minutes to 1 hour after the conclusion of your NHS appointment, or we could organise a separate visit if you would like us to. The computer safety manual lists several medical conditions, which could possibly be "affected by viewing the computer screen", however these are equivalent to viewing a television or using a computer at home. One of the vision tests uses a moving background which presents as a flickering / twinkling image, like static on a television. Therefore as a precaution, individuals with known epilepsy are excluded from this study.

If you are concerned about any potential risks, please ask and we can provide you and your child with more information.

What are the possible benefits of taking part?

This study will not directly benefit your child's vision, but your child will be contributing to our research, which is aimed at understanding and better detecting amblyopia ('lazy eye') for the future. We won't know the results of our tests until the conclusion of the project, however if we feel that any of our findings might benefit your child's individual clinical care, with your consent, we will inform your child's clinical team.

What if new information becomes available?

Sometimes in the course of a research project new information about the topic under investigation becomes available. If this occurs, we will be happy to discuss it with you, so please ask if you have questions at any time. You are always free to continue participating in our study, or you may wish to withdraw without any negative consequence.

What will happen when the research study is completed?

If you would like us to, we will send written information about our study's overall findings to you once it is completed, in clear, understandable language.

What if something goes wrong?

There are minimal risks involved in your child taking part, similar to those experienced during a normal eye test, or in watching television. If someone is harmed during the study, there are no special arrangements for compensation. If you have any concerns about this study please e-mail Mrs Louisa Haine at lah222@pgr.aru.ac.uk or phone her on 01223 698584. Alternatively email her Supervisor Dr Sarah J Waugh at s.j.waugh@hud.ac.uk or phone her on 01484 422288. We will do our best to answer your questions.

Will data collected in this study be kept confidential?

All personal information collected about your child for the purposes of the research project will be treated in strictest confidence. It will be stored securely during the project, accessible only to members of the research team, after which physical copies will be destroyed (6 months after the conclusion of the study). Digital anonymised copies will be encrypted, stored on University protected space for up to 20-years, and only accessible to the research team.

If your child joins the study, some parts of their records and data collected will be looked at only by authorised persons (the researcher and members of your child's clinical team). The hospital eye care team and your child's GP will be notified that your child is taking part in the research study, but they will not know about the specific results generated.

What will happen to the results of the research study?

The data measured on your child will be stored using an unidentifiable code from the outset, so that no-one outside the research team will know from which person the data comes from. Results of this study may be reported at scientific meetings or appear in scientific publications, but your child's data will never be identifiable to them personally. It will be averaged with data from others, and will only use an anonymous code as an identifier. Anonymised data only will be stored digitally, where it can be shared for the benefit of the future researchers and may be used for future analysis and additional research.

Who is organising and funding the research?

The project is organised and funded by Anglia Ruskin University, Cambridge. Some funding is available to offer you a £10 Amazon voucher as compensation for your time each time you participate.

Who has reviewed the study?

Ethical approval for this study has been given by an independent group of people, called a Research Ethics Committee, to protect you and your child's safety, rights, wellbeing and dignity. This study has been reviewed by Anglia Ruskin University's Faculty of Science and Technology Research Ethics Panel, and also by an NHS REC panel. If you have any complaints or concerns about your childs treatment before, during or after this study then you should contact the Chair of the Faculty of Science and Technology Research Ethics Committee, Professor Peter Bright (peter.bright@aru.ac.uk).

Contact for further information:

If you or your child have any questions regarding any aspects of this study, please e-mail Mrs Louisa Haine at lah222@pgr.aru.ac.uk or phone her on 01223 698584. Alternatively, please email her Supervisor Dr Sarah J Waugh at s.j.waugh@hud.ac.uk or phone her on 01484 422288.

Thank you for taking time to read this information

YOU WILL BE GIVEN A COPY OF THIS FORM TO KEEP, TOGETHER WITH A COPY OF YOUR CONSENT FORM.

The conduct of this study has been approved by the Faculty of Science and Technology Research Ethics Panel (FREP), Anglia Ruskin University, and by an NHS Research Ethics Committee (REC).

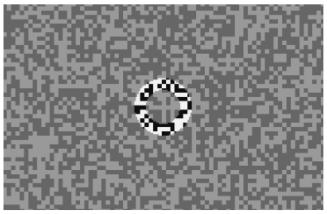
Participant Information Sheet

Title: 'New visual acuity and crowding tests for better detection of amblyopia.'

IRAS project ID: 238449

Hello,

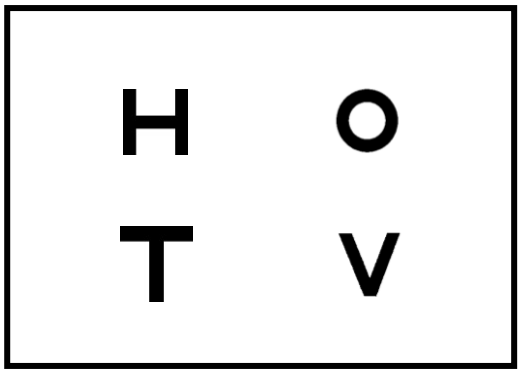
I am learning about how some children's eyes see different letters and numbers. I want to try to help improve the eye tests we use and would like you to help me.



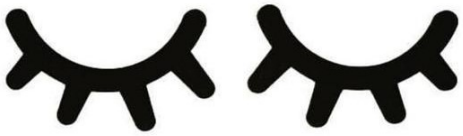
I would like you to look at some of these letters and numbers on a computer screen with one eye covered and tell me what you think they are. You may also look at some letters on a chart and some 3D pictures.

If you normally wear glasses, you should keep them on.

Do not worry if you cannot remember the name of the number or letter, because you can point to it on a card instead. If you need to guess, that is ok too.



All of these tests are safe and should not hurt your eyes, but we will have lots of rests between your games to make sure you do not get tired.



Have a talk with your parent / guardian about whether you would like to join in and if you have any other questions, do please ask.

Thank you for your help.

Louisa Haine: LAH222@pgr.aru.ac.uk

Tel: 01223 698584

My Teacher:

Dr Sarah J Waugh: s.j.waugh@hud.ac.uk

Tel: 01484 422288

Cambridge University Hospitals NHS
NHS Foundation Trust

a.r.u. | Anglia Ruskin University

CONSENT FORM FOR PARENT/GUARDIAN

Project Title: New visual acuity and crowding tests for better detection of amblyopia.
IRAS project ID number: 238449

Name of child: _____

Main investigator and contact details: Mrs Louisa Haine, Postgraduate Researcher, Anglia Vision Research, Vision and Hearing Sciences, Telephone: 01223 698 584, Email:lah222@pgr.aru.ac.uk

Research Supervisor: Dr Sarah J Waugh, Telephone: 01484 422288, Email:s.j.waugh@hud.ac.uk

1. I agree for my child/children to take part in the above research. I have read the information sheets provided (Version 6.0 – 17/02/21). I understand what my child's role will be, and all my questions and those of my child have been answered to our satisfaction.
2. I understand that I am free to withdraw my child from the research at any time, for any reason and without prejudice.
3. I understand that I am, and my child is, free to ask questions at any time during this study.
4. I have been provided with a copy of this form, the Parent's Information Sheet and the Child's Participant Information Sheet.
5. For the purposes of this research, I consent to the researchers contacting my child's ophthalmology clinical team and reviewing the medical notes, to find out information that relates to my child's visual status, spectacle prescription and binocular vision status; and for my child's GP to be informed of their participation.
6. I have been informed that the confidentiality of the information provided on behalf of my child will be safeguarded. I understand that data collected from this study will be anonymised and used for publication and sharing only in anonymised format.

Data Protection: I agree to the University processing personal data which I have supplied. I agree to the processing of such data for any purposes connected with the Research Project as outlined to me.

Name of parent or guardian (print)……

Signed…… Date……

PLEASE SIGN AND RETURN ONE COPY AND KEEP THE OTHER

If you wish to withdraw your child from this study, please speak to the researcher or email her at lah222@pgr.aru.ac.uk or her research supervisor at s.j.waugh@hud.ac.uk stating the title of the research. You do not have to give a reason for why you would like to withdraw.

The conduct of this study has been approved by the Faculty of Science and Technology Research Ethics Panel (FREP), Anglia Ruskin University, and by an NHS Research Ethics Committee (REC).

Child's Assent form

(To be read aloud to the child)

Title: 'New visual acuity and crowding tests for better detection of amblyopia.'

IRAS project ID: 238449

Hi. My name is **Louisa.** I am a scientist who is trying to learn about how we see. I am interested in how children like you see letters and numbers on a vision chart.

If you agree to be in my study, you will play a game looking at pictures of some letters and numbers on a computer screen. You may also look at letters on a chart and some 3D shapes. Sometimes they will be easy to see and sometimes hard to see.

I will ask you to tell me what you see, or you can just point to find a similar picture on my card. You will only be asked to do this for a few minutes at a time, and we will have lots of rests in between.

There are no wrong answers. Just tell me what you think you see.

By being in our study, you will be helping me to understand how children who have eyes like yours, see.

Please have a think, or talk to your parent/carer to help you decide if you want to help us. I will also ask your parent if it is OK for you to take part, but even if they say "yes," you can still say "no" if you don't want to. No one will be upset if you don't.

Even if you want to start, and then decide to stop, that is okay too. Also, remember that no one else outside the room will know what you have said.

Do you have any questions that you would like to ask me?

If you have a question later that you did not think of now, you can call me or my teacher, Dr Waugh, at (01223) 698 386 or email her at sarah.waugh@aru.ac.uk .

Would you like to be a part of my study and look at some pictures now?

☐ Participant gives clear verbal assent (and can tick the box if they want to) in presence of Guardian. Only a definite yes will be taken as consent to participate. Date

.....

The conduct of this research project has been reviewed and approved by the Faculty of Science and Technology Research Ethics Panel (FREP), Anglia Ruskin University, and a NHS ethics panel

Coversheet

Participant name: _____

Participant contact details (phone and/or email): _____

Participant information sent Y / N

Research date booked: _____

Participant consent received & filed Y / N

Parent / guardian consent received & filed Y / N

Parent been given copies of consent forms Y / N

Participant number assigned: _____

Put on database Y / N

Allocated testing group: Y / N

Testing completed: Y / N

Excluded from study Y / N

Results uploaded to database: Y / N

Clinician Letter Sent: Y / N
Date……..

Parent / guardian sent research findings: Y / N
Date……..

Parent wishes to claim for travel / parking Y / N

Reimbursed Y / N

Amount - £……..

Amazon voucher offered instead Y / NA

Amazon voucher accepted Y / N

Voucher code……..

Date participant withdrew consent: ……

Data Collection Sheet

Date:

Participant number: Visit number:

Age in months:

Gender: M / F

Recruited group - delete as appropriate:

Control / Anisometropic Amblyopia/ Strabismic Amblyopia

Refractive error:

Last clinically tested SLT date:

Visual acuity - RE: LE:

Amblyopia density – delete as appropriate:

NA / Mod amblyopia (<0.600 IOD) / Severe amblyopia (>0.600 IOD)

Current occlusion regime:

Allocated group:

Control RE leading / Control LE leading

Amblyopic eye leading / Fixing eye leading

PARTICIPANTS REQUIRED FOR RESEARCH INTO NEW VISION TESTS FOR BETTER DETECTION OF AMBLYOPIA OR "LAZY EYE"

We are looking for patients aged between 3 and 11-years-old to take part in a piece of research examining a new type of vision test, which we expect will be better at detecting and monitoring amblyopia or "lazy eye", as it is commonly known.

If you are attending an Addenbrooke's eye appointment, your child may be invited to take part. As a participant in this study, your child would be asked to complete a series of different vision tests, in the form of a game. They would be required to complete each test with each eye individually, similar to how their eyes are tested during their clinical appointments.

It should take no longer than one hour (60 minutes) to complete all the tests, depending upon your child's age and attention span, but might be as short as 30 minutes. We can also arrange for the tests to occur after your child's routine clinic appointment, in order to minimise disruption to their timetable.

An Amazon voucher of £10 is available for each involvement, as compensation for your time and travel expenses.

For more information about this study, please speak to a member of your clinical team or contact;

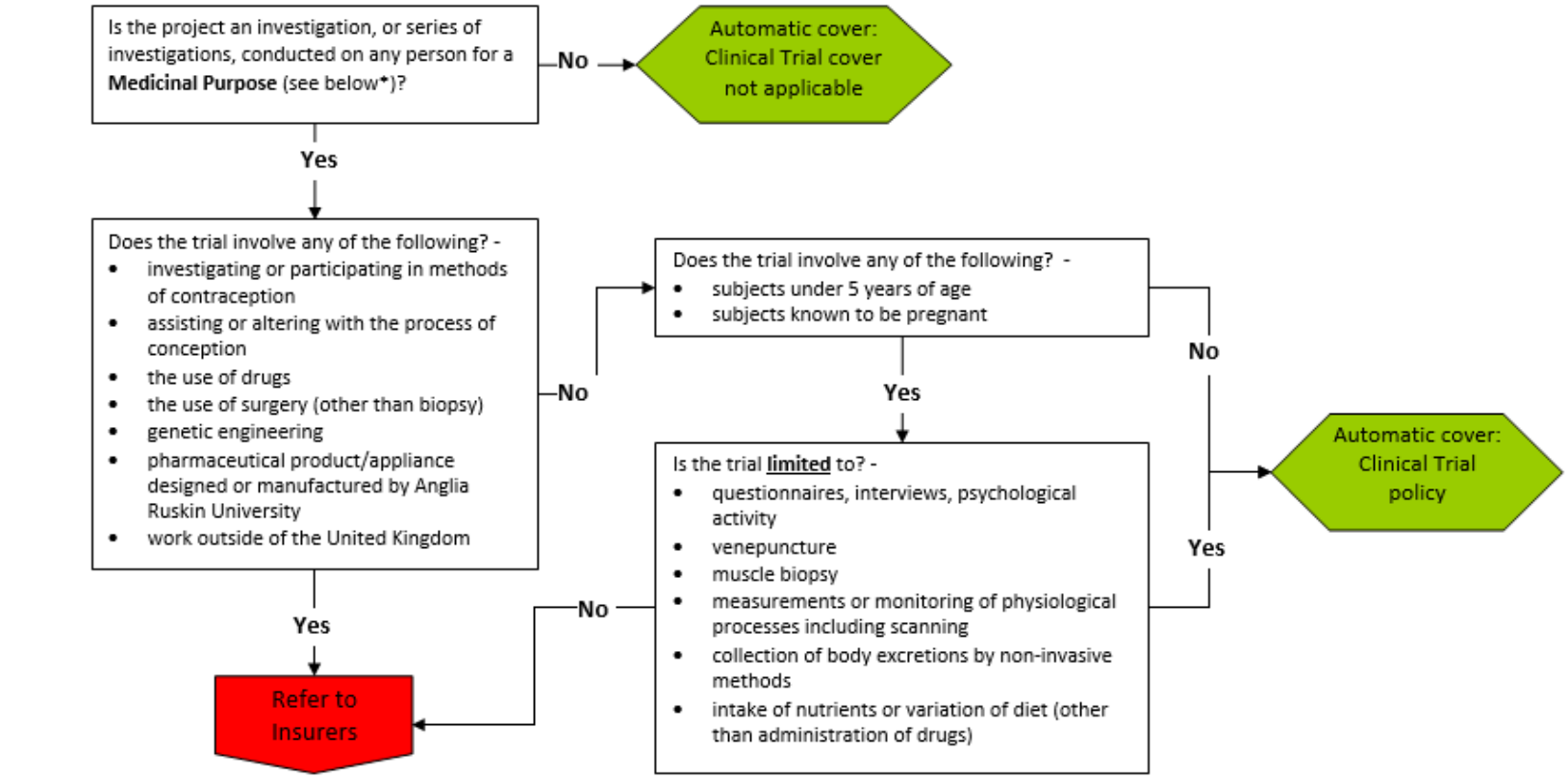
Louisa Haine – Postgraduate Researcher

Faculty of Science and Technology, Anglia Ruskin University

Email: LAH222@pgr.aru.ac.uk

Ethical approval for this study has been granted by Anglia Ruskin University and an NHS research and Ethics committee.

Research involving Human Participants (Clinical Trial) Project Referral Map



***Medicinal Purpose** means:

a) treating or preventing disease or diagnosing disease or
b) ascertaining the existence degree of or extent of a physiological condition or
c) assisting with or altering in any way the process of conception or
d) investigating or participating in methods of contraception or
e) inducing anaesthesia or
f) otherwise preventing or interfering with the normal operation of a physiological function

Appendix 2

COVID-19 Contact Tracing Consent Form for face-to-face Research (from ARU's Data Protection Officer).

As part of ARU's management of COVID-19 risks I am required to ask you for your name and contact number, and your consent for me to keep this information for 21 days in line with Government Guidance. This is to support Test & Trace activity in the event that participants in this research are at risk of having come into contact with an individual with positive case of COVID-19.

Please read the Privacy Notice below and overleaf, and if you wish to, please provide your details and your signature confirming your consent.

You are under no obligation to provide this information. However we will not be able to include you in the research without it.

□Full name:	
Contact Details (home or mobile phone number):	
□I have read the ARU Privacy Notice for COVID-19 Management and consent to ARU holding my information for this purpose:	
Signature:	
Date:	

□

Privacy Notice for COVID-19 Management

This Privacy Notice is designed to help you understand how we use personal information for this initiative. We have set out below the information we use, who we share it with, and how long we will keep it.

What is covered by this privacy notice?

Collecting, storing and sharing your personal data for the purposes of managing the University and Community response to the COVID-19 pandemic. Applies to University staff, students, and other visitors to campuses and other venues being used for University purposes.

What personal information will we hold?

• Your name, contact details, dates and times when present on campus. See Government Guidance: https://www.gov.uk/guidance/maintaining-records-of-staff-customers-and-visitors-to-support-nhs-test-and-trace

How do we use your personal information?

We use this information for these purposes:

To inform you if we become aware of a positive case with whom you may have been in close contact to allow us to give you further guidance.

To support the Local Authority and Health Protection Teams in taking additional measures to manage the spread of the pandemic.

Who else might we share your personal information with?

We will securely share the identifiable data above about cases and potential contacts with Local Authority Public Health and Health Protection Teams.

Who is the data controller for this processing?

Anglia Ruskin University is the Data Controller. Where we share personal data, the receiving authority will also become a Data Controller.

What is the legal basis for our use of your personal information?

Your consent

How long will we keep your personal information?

21 days in line with government guidance

Your rights

The law gives you a number of rights to control what personal information is used by us and how it is used by us.

You can obtain further information about these rights from the Information Commissioner's Office.

You also have the right to lodge a complaint in relation to this summary notice, the full Privacy Notice or our processing activities with the Information Commissioner's Office. Information Commissioner's Office Post: Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire SK9 5AF

Website: https://ico.org.uk/ Email: casework@ico.org.uk

Telephone: 0303 123 1113 (local rate) or 01625 545745 (national rate)

Contact us

If you wish to exercise any of these rights, you can contact our Data Protection Officer. Data Protection Officer

Email: dpo@aru.ac.uk

Appendix 2 – Schedule of Procedures

Procedure	Visit			
	ACPOS clinical appointment	First visit	Second visit (If participant opts in)	Third visit (if participant opts in)
Participant identification and dissemination of information sheets	x			
Consent and Assent		x		
Background and medical history		x	x	x
Completion of modified visual acuity tests		x	x	x

Appendix 3 – Amendment history

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made