PROTOCOL

The Role of Glasses Wearing in Amblyopia Treatment
A Randomised Controlled Multicentre Trial

Acronym: **EuPatch** (**Eu**ropean **P**aediatric **A**mblyopia **T**reatment study for **Ch**ildren)

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Summary/Abstract

Background: Amblyopia (also called lazy eye) is the most common disease affecting vision in childhood. It affects between 2 to 5% of the population and 90% of visits to children's' eye clinics are for the purpose of treating amblyopia. Currently 30% of children treated for amblyopia do not reach normal vision after a year or more of treatment. Amblyopia is usually treated with glasses wearing and by patching the better eye.

There is controversy whether a long period of glasses wearing before patching, called refractive adaptation, helps in treating children with amblyopia. Refractive adaptation has not been tested in a randomised controlled trial, and currently we do not know how long children wear glasses each day.

Objectives: The purpose of this study is to perform the first randomised controlled trial to test whether refractive adaptation before patching improves the number of successfully treated children with amblyopia. We will use electronic monitors to measure how much children wear their glasses and patches each day and will determine how this relates to their improvement in vision. We will also investigate whether different types of amblyopia respond better to different treatments.

Clinical benefits: This trial should clarify whether refractive adaptation is a better treatment option for improving the number successful treated children with amblyopia or not. It should also help to find out how long children wear glasses each day and whether poor compliance is a problem that hinders the improvement in vision.

Introduction

Background

Amblyopia (or lazy eye) is the most common visual disease in childhood affecting an estimated 2 to 5% of the population.[1,2] If left untreated amblyopia can lead to serious visual impairment in one eye and occasionally both eyes. Amblyopia is associated with disrupted development of the visual brain areas. Amblyopia is caused by unequal inputs from the two eyes during visual development in childhood, usually either because of an eye turn (strabismus), a difference in refractive properties of the two eyes (anisometropia), or a combination of both (mixed amblyopia). Amblyopia also carries an increased life time risk of serious loss of vision to the better eye of between 1.2 and 3.3%.[3]

Treatment of amblyopia accounts for approximately 90% of visits to children's' eye clinics.[4] Current outcomes of patching treatment for amblyopia in the NHS are poor, with 30% of children not reaching normal visual acuity, but remaining at 6/12 or worse in the amblyopic eye after a year or more of treatment and several thousand hours of prescribed patching treatment.[5] Optimising amblyopia treatment regimes is, therefore, crucial for improving vision in children with amblyopia and reducing ineffective treatment in the NHS. Better treatment regimes would also provide considerable cost-benefits to health services and make amblyopia treatment less burdensome for children and families.[6]

Amblyopia is usually treated firstly with glasses wearing, to correct for the refractive errors existing in most amblyopic children, followed by patching the "better seeing" eye, forcing the brain to use the amblyopic eye. Several studies indicate that vision can improve significantly during the glasses wearing period before patching treatment commences.[7-12] This has led to the idea that an extended period of glasses wearing, called refractive adaptation (or RA), should be prescribed to all amblyopic children before patching begins.[9] The rationale behind this is to improve vision through glasses wearing alone in order to reduce the distress caused by patching or in some children avoid patching altogether.

Current guidelines from the Royal College of Ophthalmology (2010 NHS Annual Update on Amblyopia) recommend 16-22 weeks of RA.[13] However, the role of glasses wearing in amblyopia treatment is poorly understood. No studies have yet directly compared patching treatment with and without RA in order to show that RA either reduces the number of hours of patching required or improves final visual outcome. Also, compliance to glass wearing during RA and the effect of RA on compliance to the patching treatment that follows has never been investigated.

Own work related to the proposed study

Pilot Work performed by the Leicester Ophthalmology Group

Progress has been made in understanding the role of patching in amblyopia treatment using electronic dose monitors. These are miniature data loggers that measure the amount of patching by monitoring the temperature difference between the surfaces of the device. We, along with other groups[14-18] have used electronic monitors: (i) to show that compliance to prescribed patching regimes is highly variable and is a major factor in the success of amblyopia treatment (figure 1&2), (ii) to determine the dose-response relationship between patching treatment and improvement in vision (figure 1), and (iii) to show that compliance to patching can be improved using educational/motivational materials (figure 2). Our studies indicate that an intense patching regime (10 hours/day, 6 days/week) supplemented with an educational/motivational intervention is an efficient and cost-effective way of increasing the number of hours children patch for.[15] This approach hastens improvement in vision compared to low intensity regimes reducing the number of clinic visits required by amblyopic children, which is currently by far the greatest cost in amblyopia treatment.[5]

We have recently piloted electronic glasses wearing monitors for the first time. The glasses dose monitor is taped to the frame of the glasses in close proximity to the temple (Figure 3A). Output from the monitor showed an excellent signal to noise ratio (figure 3B). To date we have made 110 continuous 42 day long recordings with a 100% success rate. In feedback from the pilot study, parents expressed a concern over the size of the monitor. As a result the monitors have been redesigned to be 40% smaller in volume than the previous version (27 x 11 x 4.5mm, figure 3C).

In the pilot study we recruited 22 children (11 anisometropes, 4 strabismic, 7 mixed) to investigate compliance to glasses wearing during amblyopia treatment. Glasses wearing was monitored continuously over an 18-week period (at 10 minute intervals) with visual acuity (VA) measured using logMAR crowded (Glasgow acuity) charts at 6 week intervals. Figure 4 illustrates the wide range of compliance with glasses wearing recorded ranging from 17% to 99% of all hours awake. Over the 18-week period of glasses wearing there was a clear dose-response between the numbers of hours of glasses wearing per day and improvement in VA in the amblyopic eye (figure 5, R=0.75, p<0.0001). The data suggests that optimal responses are obtained from full-time (12 hours/day) glasses wearing and that most patients show sub-optimal levels of compliance. Amblyopia was successfully resolved in only 1 of the 22 patients after 18 weeks RA. These results are in agreement with those of Stewart et al.[18] who

find that RA is a relatively weak form of treatment with only 7 out of 93 patients improving to the point where they did not need further treatment after 18-weeks RA.

The 18-week glasses-wearing period was followed by a combined patching (10 hours/day, 6 days/week), and glasses wearing monitoring period of 12 weeks (i.e. 720 hours of prescribed patching). This matches the protocol of a previous study we performed without extended RA[15] allowing a preliminary comparison of visual outcomes with and without an extended 18-week period of RA. Figure 6 illustrates the comparison and demonstrates that although the final visual acuity in the amblyopic eye is similar with and without RA; 36.4% of patients were successfully treated after the 12 week patching period when RA was used compared to 23.1% when there was no RA. However, compliance to patching following RA was worse in the RA group, although this did not reach statistical significance (patching compliances: 5.8 hours/day in the RA group and 6.7 hours per day in the non-RA group).

Rationale for Proposed Study

Our preliminary results suggest that RA could be an effective way of significantly improving the number of patients successfully treated after a fixed amount of prescribed patching. However, the role of RA is controversial since RA could also impede compliance to patching therapy overall as the treatment is longer and patients/parents may become less motivated. There have been no randomised controlled trials to test these questions objectively, which is the main aim of this study.

Although not the primary objective we will also explore a number of other questions in the study. We have found a significant dose-response *relationship* between patching treatment and improvement in vision in children with strabismic and mixed amblyopia but not anisometropic amblyopia (figure 1). This raises the possibility that RA may only be more effective in anisometropia since some patients who only patched a few hours showed 100% improvement in vision (figure 1B). Another issue is that using electronic monitors could also affect compliance and influence visual improvement. No study to date has examined the effect of monitoring on compliance in amblyopia and improvement in vision.

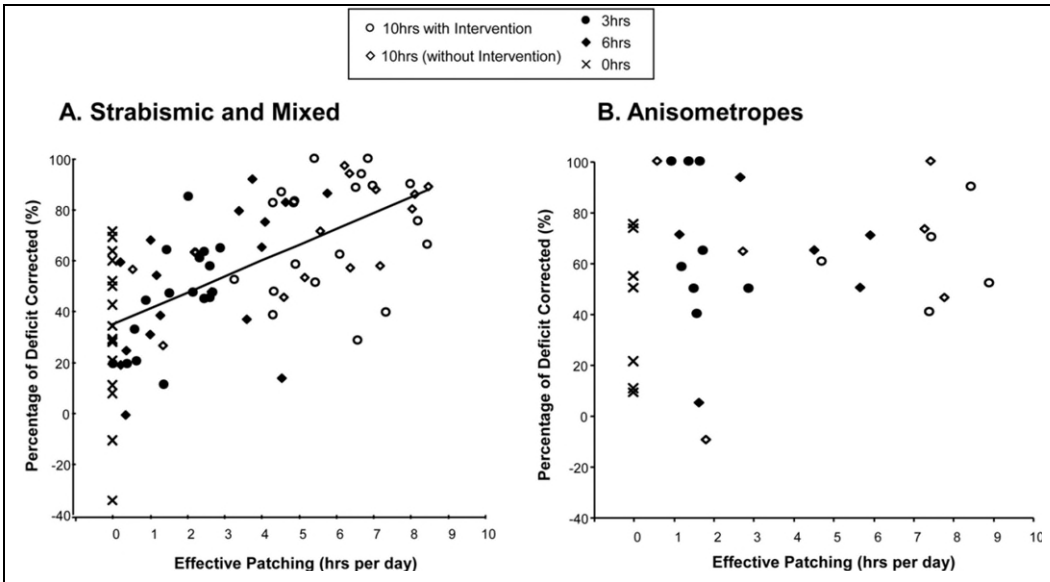
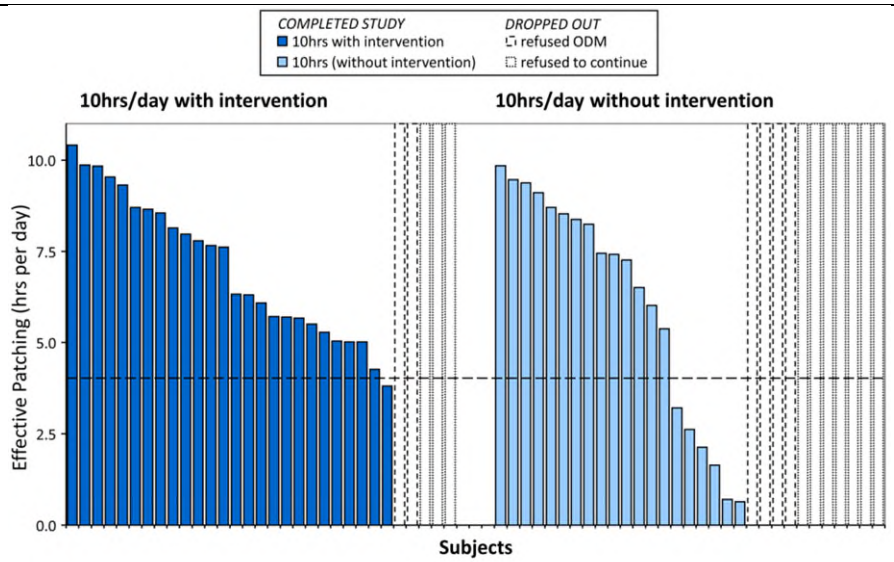


Figure 1. *Data from two of our studies[14,15] showing the dose-response relationship between effective patching (electronically monitored) and improvement in vision. The dose-response relationship is clear for (A) strabismic and mixed amblyopes but not for (B) anisometropes. Patients were prescribed various doses (shown in the key and some received an educational/ motivational intervention - see figure 2).*

Figure 2: *Results from a study we recently completed using occlusion dose monitors which were used to test the effect of an educational/motivational intervention on patching compliance.[15]*
Greater numbers of poor compliers (<4hours patching) and drop outs (dashed and dotted empty bars) were present in the group that did not receive the educational/motivational intervention



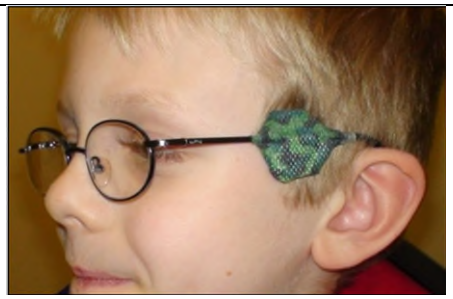


Figure 3A (left): *The glasses dose monitor used to measure compliance to glasses wearing in the pilot study.*
Figure 3B (below). *Output from a glasses dose monitor over a 42 day period. Values above the dotted line indicate periods of glasses wearing.*

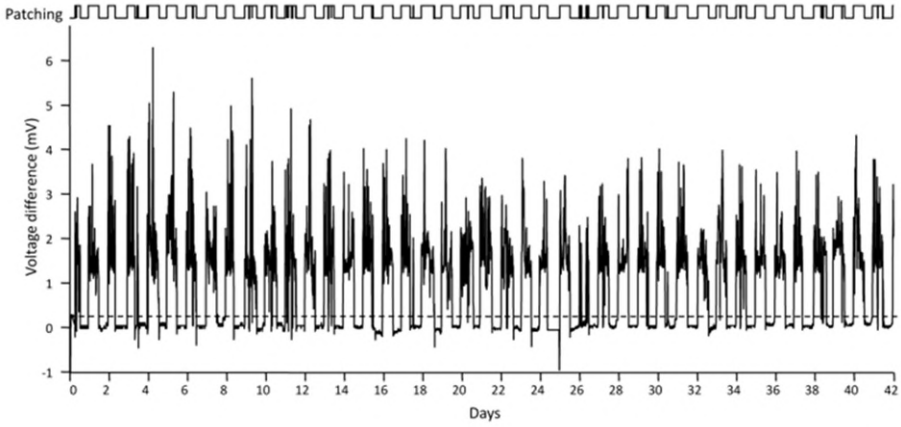


Figure 3C (below). *The newly redesigned (40% smaller) glasses dose monitor which is 27 x 11 x 4.5mm.*

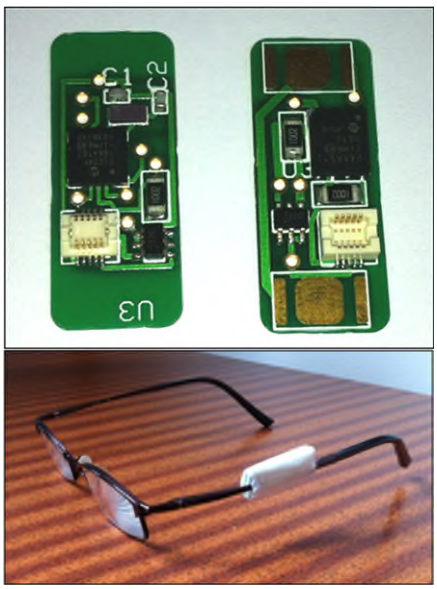


Figure 4. *Compliance to glasses wearing during refractive adaptation from pilot study for children prescribed all waking hours (arranged in order from best compliance to worst compliance). Compliances ranged from 17% to 99%.*

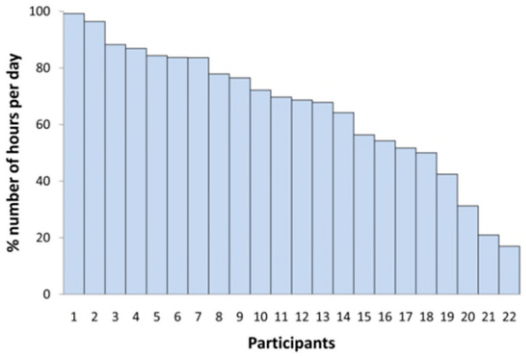
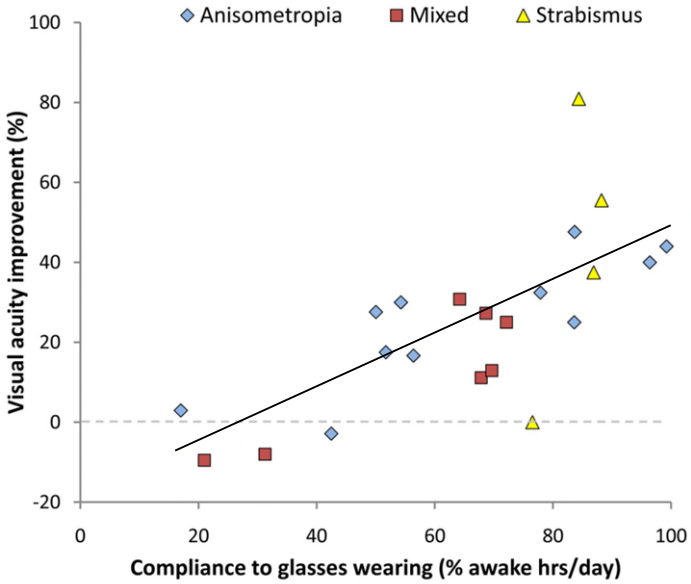
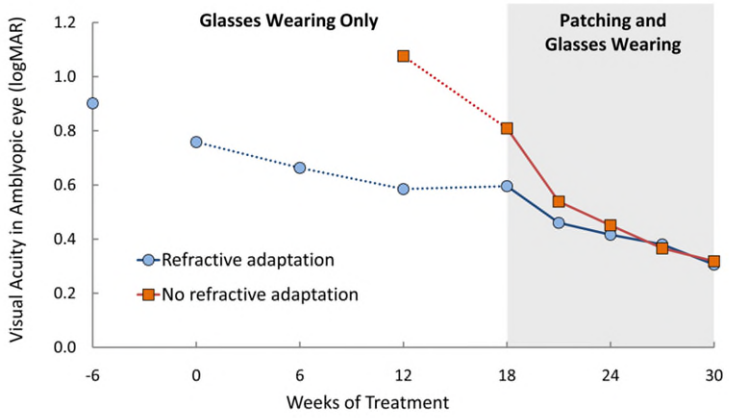


Figure 5. *The relationship between improvement in visual acuity (as a % of amblyopic deficit before treatment) and compliance to glasses wearing during refractive adaptation for children prescribed all waking hours. A clear dose-response relationship is evident (*R*=0.75,* p*<0.0001). Little improvement is seen below 40% compliance and 100% compliance achieved only approximately 43% improvement in vision.*





% total number resolved (reaching 0.1 logMAR in amblyopic eye)

	0 wks	*6 wks*	*12 wks*	*18 wks*	*24 wks*	*30 wks*
Refractive Adaptation	0	0	0	4.55	18.18	36.36
No Refractive Adaptation				0	7.69	23.08

Figure 6. *Improvement in visual acuity in the amblyopic eye with and without a period of refractive adaptation (comparing pilot data to data from a previous study). The final visual acuity was similar in both cases although treatment took much longer with RA. However, a larger proportion of patients were resolved (visual acuity in the amblyopic eye reaching 0.1 or better) for the same amount of patching using RA.*

Hypothesis and research questions

The number of children successfully treated after 720 hours of prescribed patching over 12 weeks following an initial period of 18 weeks glasses wearing prior to patching weeks will be significantly higher than after an initial period of 3 weeks glasses wearing prior to patching therapy.

Research questions

Primary research question:

Does the number of children successfully treated after 720 hours of prescribed patching over 12 weeks following an initial period of 18 glasses wearing (refractive adaptation group) prior to patching improve significantly compared to children receiving an initial period of glasses wearing of 3 weeks (early patching group) prior to patching therapy?

Secondary research questions:

The secondary outcome measures will be exploratory

1. a) Does the number of patients successfully resolved ≤ 1080 hours of prescribed patching over 18 weeks differ between the refractive adaptation group and early patching group?
   b) Does the number of patients successfully resolved ≤ 1440 hours over 24 weeks differ between the refractive adaptation group and early patching group?

2. What are the levels of compliance to glasses and patch wearing?

3. Is there a relationship between duration of glasses wearing and patching and improvement in vision?

4. Do anisometropes respond better to refractive adaptation (RA) compared to strabismus/mixed patients?

5. Does electronic monitoring influences compliance and visual outcomes?

6. Do children and carers have a subjective preference to longer periods of glasses wear?

Aim

Primary objective:

To perform a parallel two-armed randomised controlled trial to compare the number of children successfully treated after 720 hours of prescribed patching over 12 weeks following an initial period of either 3 weeks or 18 weeks glasses wearing prior to patching therapy.

Definition of successful treatment: visual acuity in the amblyopic eye reaches ≤ 0.1 logMAR difference from the better eye

Secondary objectives (exploratory investigations)

The secondary outcome measures will be exploratory

1. To compare the number of patients successfully resolved in ≤ 1080 hours of prescribed patching over 18 weeks, and in ≤ 1440 hours over 24 weeks. Where possible we will also compare the two groups in terms of final visual outcome, total duration of treatment and total amount of patching required.

2. To estimate the levels of compliance to glasses and patch wearing.

3. To explore the relationship between duration of glasses wearing and patching and improvement in vision.

4. To explore whether anisometropes respond better to RA compared to strabismus/mixed patients.

5. To explore whether electronic monitoring influences compliance and visual outcomes

6. Ascertain opinions from carers and children about the study treatment study through a questionnaire given during and on completion of the study.

Methods/Protocol

Type of study:

Unmasked randomised controlled trial comparing amblyopia treatment with and without prolonged refractive adaptation.

Subjects:

A. Refractive Adaptation Group: A period of **18 weeks** glasses wearing (i.e. RA) will be followed by a period of 24 weeks combined patching (10hrs/day, 6 days/week) and glasses wearing (n=173).

B. Early Patching Group: A period of **3 weeks** glasses wearing will be followed by a period of 24 weeks combined patching (10hrs/day, 6 days/week) and glasses wearing (n=173).

Recruitment:

Subjects will be recruited from paediatric ophthalmology/orthoptic outpatient clinics as well as with posters and leaflets placed in clinics.

Inclusion criteria:

Inclusion criteria are children with newly detected amblyopia (difference of ≥ 0.3 logMAR visual acuity between eyes), a clinically significant refractive error (≥ 1.5D in at least 1 eye or 1D difference between the two eyes) and able to perform the visual acuity test (aged 3 to 8 years).

Exclusion criteria:

Exclusion criteria are children without amblyopia as defined above or with amblyopia as defined above but with other ophthalmic or neurological diseases, or premature children. Bilateral amblyopia (visual

acuity of the sound eye with best corrected visual acuity of greater than 0.3 (6/12) LogMAR) is also an exclusion criterion.

Withdrawal Criteria:

Patients may be withdrawn from the study by the investigator at any time for the following reasons:

- Non-compliance in major issues
- The patient is found not to satisfy exclusion/inclusion criteria

Patients must be withdrawn from the study by the investigator at any time for the following reasons:

- Inability to continue participation in the trial for other medical reasons (i.e. ill health)
- Withdrawal of informed consent by the participant
- Any other condition which in the opinion of the investigator no longer justifies or allows the safe participation of the participant

Participants may withdraw their consent from the trial at any time without affecting their standard clinical treatment. Reasons for premature withdrawal will be documented in the site file.

Safety Reporting Procedures:

An *adverse event* is any untoward medical occurrence in a participant who has been administered an intervention. This includes occurrences that may not be caused or related to the product.

An *adverse reaction* is any untoward and unintended response in a participant to the investigational intervention. This is related to any intervention administered to a participant and is known as an adverse reaction to the intervention.

A *suspected unexpected serious adverse reaction* (SUSAR) is a serious adverse reaction that is unexpected. The nature and severity is not consistent with the information about the intervention. An *adverse event* or *adverse reaction* is serious if it:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

Medical judgement will be exercised in deciding whether an *adverse event/adverse reaction* is serious and/or unexpected.

A *serious adverse event* (SAE) occurring to any participant will be notified to the University of Leicester (UoL)(sponsor) within 24hrs of the Principal investigator (PI) becoming aware of the event. This is reported by submitting the latest version of the UoL Safety Reporting Form which is then faxed/emailed to UoL Research Governance office, followed by a hard copy, signed by the PI. At the Research Governance office this is registered onto a database and reviewed by to ascertain whether the SAE was likely to be related to the involvement in the trial. A letter is issued by the UoL Research Governance office noting that it has been reviewed.

A *serious adverse reaction* (SAR) and *suspected unexpected serious adverse reaction* (SUSAR) will be reported to the UoL Research Governance office within 24 using the UoL Safety Reporting Form. Only SUSARs need to be reported to the Ethics Committee. The responsibility to identify whether the reaction is a SUSAR is that of the Chief/Principal Investigator. The UoL Research Governance office will report the SUSAR to Ethics. Any increase in severity of the reaction or event will be reported to the

Research Governance office. Requests for further information from the Ethics Committee will be submitted to them within 8 days.

Annual Safety Reports of SUSARs and SARs will be filled out by the PI. The annual Safety Reports will be forwarded to the Research Ethics Committee by the UoL.

All Safety Report Forms and relevant information will be filed in the Site File and will be reported on the appropriate Case Report Form.

Information and consent process for human studies:

Parents or guardians who are interested in the study will be given the patient information sheet and verbal information by one of the investigators. They will have a minimum of twenty-four hours to read the information leaflet. If they wish, they will be able to contact one of the investigators to obtain further verbal information. If they agree to participate in the study, they will need to sign the written consent form. A simple information leaflet will be prepared for older children and if they like they can give assent.

Assessment of statistical power:

The sample size is based on our previous study[15] in 62 patients, where the number of amblyopic children resolving after 12 weeks of patching treatment (10 hours/day, 6 days/week) was 23% without RA. To show a clinically significant improvement in success rate of 15% using RA would require 173 patients in each arm (α=0.05, power = 80%, drop-out rate = 15%).

Statistical Analysis:

The outcome and secondary outcome measures will be compared using a Chi-square test with drop-outs considered as failures to allow an intention-to-treat analysis. Dose-response relationships will be modelled using regression analysis in the different types of amblyopia.

Details of research performed:

Prior to commencing the study all children will undergo a full orthoptic and ophthalmological examination including visual acuity (Glasgow acuity carts), cover test, ocular motility, binocular vision (Frisby test and Bagolini test), slit lamp examination and funduscopy. Optimal refraction will be determined using cycloplegic refraction (normally after instillation of 1% cyclopentolate, if pupils do not dilate for example if patients have dark irides additional drops will be instilled at the discretion of the examiner). A socioeconomic questionnaire will also be given to the guardians or parents at the beginning of the study.

An educational intervention which has been shown to improve compliance[15] will be given to all children and parents and guardians at the beginning of the study.

During RA children will be requested to wear glasses during all waking hours for 18 weeks (refractive adaptation group) or 3 weeks (early patching group).

Children will then be asked to patch 10 hours/day for 6 days/week for 24 weeks in addition to continue to wear their glasses.

Children will be examined every 6 weeks by the research orthoptist at which point VA will be measured using logMAR crowded visual acuity tests (using Glasgow acuity cards) and binocularity will be measured (Frisby test and Bagolini test).

The amount of glasses wear and patching should adhere to the protocol whenever possible. However changes in management may be made at the discretion of the ophthalmologist / orthoptist if the amblyopic eye is successfully treated (visual acuity in the amblyopic eye reaches ≤ 0.1 logMAR difference from the better eye) before the end of the study or if adverse side effects such as increase in squint or diplopia occur.

After 12 weeks of patching and on completion of the study (24 weeks of patching), a modified amblyopia treatment index questionnaire (Lazy Eye Treatment Questionnaire) will be given to the parents or guardians[20]. A short feedback questionnaire will also be given to the children. These questionnaires will assess the patients and their carers' subjective opinion of the treatment given during the study.

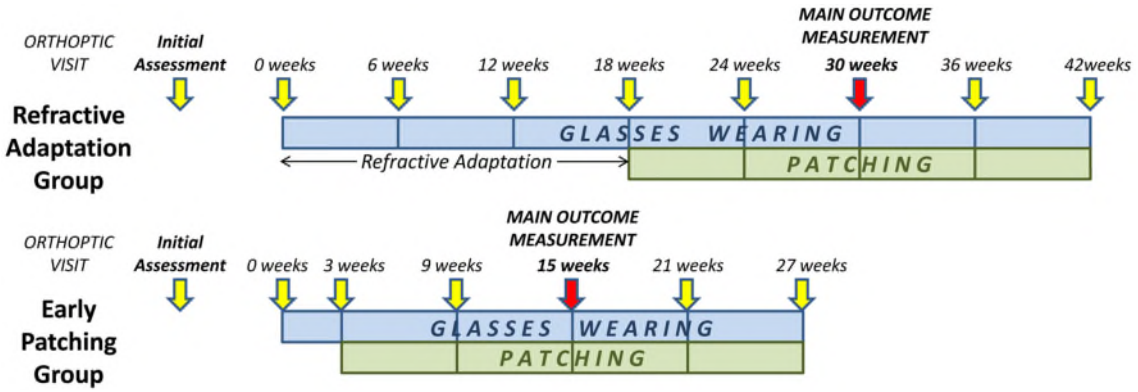
Successfully treated children (visual acuity in the amblyopic eye reaches ≤ 0.1 logMAR difference from the better eye) before the end of the study will be asked to continue to attend the appointments

Methods of monitoring occlusion: Glasses wearing and patching will be electronically monitored in 50% of children selected at random and the data will be downloaded to a PC. We have extensive experience using ODMs from previous studies.[14,15] Parents/guardians will also be asked to keep a diary of glasses and patch wearing times. Diary times and VAs will be compared between children who are electronically monitored and those who are not, to investigate the effect of electronic monitoring on compliance and visual outcomes.

Summary of examinations

346 children with newly detected amblyopia will be recruited and randomized into the two groups (refractive adaptation group and early patching group) stratified by type of amblyopia and by severity of amblyopia (VA above and below 0.5 logMAR). In each stratified group 50% of children will be randomised to wear glass and occlusion dose monitors to investigate compliance.

Overview of Study Design:



Refractive adaptation group

VISIT/DAYS **EXAMINATION 1**

Initial assessment	Full orthoptic/ophthalmological examination including motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test), slit lamp and fundus examination, cycloplegic refraction (1% cyclopentolate, except in children where pupils do not with dilate, for example with dark irides where additional drops can be instilled at the examiners discretion). Glasses will be prescribed at this examination. Amblyopia demographics questionnaire will also be given.
Week 0	**EXAMINATION 2** *Children wear glasses for the first time during examination at this visit.* Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor will be fixed on frames of glasses in 50% of children)
Week 6	**EXAMINATION 3** Children continue to wear glasses. Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor will be continue to record compliance on frames of glasses in 50% of children)
Week 12	**EXAMINATION 4** Children continue to wear glasses. Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor will be continued on frames of glasses in 50% of children)
Week 18	**EXAMINATION 5** *Children continue to wear glasses and start patching (occlusion dose monitor will be placed on patches in those children who have used glass dose monitor)*

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor will be continued on frames of glasses in 50% of children)

Week 24 **EXAMINATION 6**

Children continue to wear glasses and start with patching.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them)

Week 30 **EXAMINATION 7**

Children continue to wear glasses and patches.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them) and Lazy Eye Treatment Questionnaire given.

Week 36 **EXAMINATION 8**

Children continue to wear glasses and patches.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them)

Week 42 **EXAMINATION 9**

Last examination

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) and Lazy Eye Treatment Questionnaire given.

Children will be return to NHS care if needed

Early patching Group

VISIT/DAYS	EXAMINATION 1
Initial assessment	Full orthoptic/opthalmological examination including motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test), slit lamp and fundus examination, cycloplegic refraction (1% cyclopentolate, except in children where pupils do not with dilate, for example with dark irides where additional drops can be instilled at the examiners discretion). Glasses will be prescribed at this examination. Amblyopia demographic questionnaire will also be given.
Week 0	**EXAMINATION 2** *Children wear glasses for the first time during examination at this visit.* Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor will be fixed on frames of glasses in 50% of children)
Week 3	**EXAMINATION 3** *Children continue to wear glasses and start with patches (glass dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them)* Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test)
Week 9	**EXAMINATION 4** Children continue to wear glasses and patches.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them)

Week 15 **EXAMINATION 5**

Children continue to wear glasses and patches.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glasses dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them). Carers will be ask to complete Lazy Eye Treatment Questionnaire

Week 21 **EXAMINATION 6**

Children continue to wear glasses and patches.

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) (glass dose monitor and occlusion dose monitor on patches will be continued in 50% of children who have already worn them).

Week 27 **EXAMINATION 7**

Last examination

Ocular motility, cover test, logMAR visual acuity (Glasgow acuity cards), binocular vision (Frisby and Bagolini test) and Carers will be ask to complete Lazy Eye Treatment Questionnaire.

Children will be return to NHS care if needed

Evaluation of data:

Primary outcome measure:

Number of successfully treated children (visual acuity in the amblyopic eye reaches ≤ 0.1 logMAR difference from the better eye) at 12 weeks after patching has commenced will be compared using a Chi-square test with drop-outs considered as failures to allow an intention-to-treat analysis.

Secondary outcome measures:

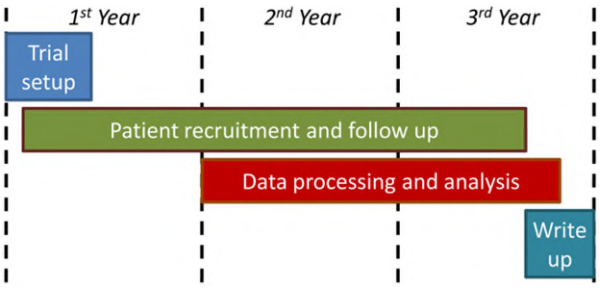
Outcome measure will be compared using a Chi-square. Dose-response relationships will be modeled using regression analysis in the different types of amblyopia.

Assessment of possible adverse side effects

Possible complications of patching can be increase of squint, double vision or decrease of vision of the better eye. This will be carefully monitored every 6 weeks. If side effects occur patching will be reduced or stopped at the discretion of the examiner.

Timing

We are aiming to start this study in March 2013 and to complete the study in three years (see timeline below).



Study end-point

Completion of all examinations in 346 patients, analysis of data and writing up of findings.

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