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## Introduction

It is well reported that children with Down's syndrome have poorer visual acuity than expected for age(1-3) even when refractive errors are corrected. Objective measurements of acuity by visual evoked potentials have shown that the deficit is not explained by lack of concentration, motivation or persistence in acuity testing(4) and other studies implicate the quality of the optics in reducing visual acuity in children with Down's syndrome(5). This may present a problem for clinicians examining children with Down's syndrome, in discriminating between an acceptable or 'normal' level of visual acuity and a poor acuity indicative of amblyopia or pathology.

Children with Down's syndrome exhibit a number of characteristics different from typically-developing children; among them is retarded growth - children with Down's syndrome are generally small for age. The Down's Syndrome Medical Interest Group, a UK and Ireland organisation of health care practitioners (mainly paediatricians), publishes growth charts specifically for children with Down's syndrome, which paediatricians can use to monitor a child's growth compared to the appropriate norms. Refractive error profiles are available for children with Down's syndrome up to the age of 15 years, but no norms for visual acuity have yet been published.

Our research group, the Down's Syndrome Vision Research Unit, has been involved in a longitudinal study of visual and ocular development of children with Down's syndrome since 1992 and we therefore have the data available to develop norms for the use of eye care practitioners. At the outset, recruitment of very young children was through paediatricians in South and West Wales, but since then we have targeted older children in the local area, at various times for specific research studies. More recently, as parents have become aware of our work, families have contacted us directly requesting to join our studies; we have no exclusion criteria for families wishing to enrol, except that the child must have a diagnosis of Trisomy 21. Although most children in the study cohort live in South and West Wales, some children travel considerable distances to take part.

Children participate in conventional eye examinations as well as in laboratory-based experiments. Over the years, eye examinations have been conducted in the children's homes, on school premises and/or in the clinic at Cardiff University School of Optometry & Vision Sciences. Clinical data include visual acuity, refractive error, accommodation, and binocular status and are available for a total of 226 participants at various ages. We therefore have ample data to establish normative values.

The longitudinal study has had continual and on-going ethical approval from the appropriate bodies covering NHS ethics in Wales (the actual institutions have changed over the 25 years of the study). Parental consent was given for all data collected and the study conducted in accordance with the Declaration of Helsinki.

## Methods

The Down's Syndrome Vision Research Unit database was used to retrospectively examine the record cards of all children seen between December 1992 and April 2017. 'Normal values' should ideally be collected from a non-clinical population, since a subject group presenting at a clinic cannot be expected to be representative of the general population. The published normal values for typically developed children (6-9) generally report on a non-clinical population, but use exclusion criteria, particularly for refractive errors, to ensure 'normal vision'. The only norms available for the Keeler Crowded test, on the other hand (10), were obtained from children referred to an orthoptic clinic, and determined to be non-strabismic. For the early years of our longitudinal study, children with Down's syndrome in South and West Wales were identified by the Cytogenetics Department of the University Hospital Wales, and then recruited through the children's paediatricians. Only two

families refused to join the study at this stage. An additional recruitment campaign was initiated for the bifocal spectacle trial (11), through Educational Psychologists, without reference to visual concerns. Children who did not go on to participate in the bifocal trial, either because they did not have an accommodative deficit, or because they could not be satisfactorily matched to another child, remained in the cohort. At this stage then, the study group of 'early' recruits was not a clinical population. Since the early 2000's, as our work has become increasingly well-known, families have contacted us directly requesting to join our studies; we have no exclusion criteria for families wishing to enrol, except that the child must have a diagnosis of Trisomy 21. Many families joining the study in this way have no prior concerns about their child's vision; nevertheless, it is possible that children joining through this route are more likely to have visual deficits. We therefore identified these children in the current analysis as 'late' recruits. Each year a large number of families from all over the UK simply request clinical appointments for their child with Down's syndrome. These children are not enrolled into the longitudinal study, although they may take part in other aspects of the team's studies.

From the database of 226 participants, children with visually-impairing conditions such as aphakia (N=1) or nystagmus (N= 39) were excluded from analysis, as were children who joined the study after the age of 12 years (N=9); 177 children remained, including those with strabismus.

The database contains data on children before they were prescribed spectacles for significant refractive errors. Those visits at which the child had uncorrected refractive error were excluded according to the following criteria. The criterion for significant hypermetropia was identical to that used for the studies of normal values of visual acuity in children, for the tests we used. For Teller cards this was  $>+5.00D$  (8), for Cardiff Acuity Test (6) and Keeler LogMAR (10) this was  $>+3.00D$  and for Kay Pictures (9)  $>+2.00D$ . Three children were excluded because there were no later visits when refraction was corrected; other children had later data after provision of spectacles. Low myopia was not considered detrimental to PL acuity, and there were no exclusions for uncorrected myopia. When distance optotype tests were used, no child had uncorrected myopia. Further exclusions (N=5) were visits on which binocular acuity data were not obtained.

The database of 159 children was then inspected without acuity data, to prevent any bias, and children were allocated to age groups. Grouping was at 6-monthly intervals for up to 2 years, since acuity is expected to change rapidly in infancy. Thereafter, grouping was two-yearly up to 11.9 years. The following 9 age groups were created:

1-5.9 months, 6-11.9 months, 12-17.9 months, 18-23.9 months, 2-3.9 years, 4-5.9 years, 6-7.9 years, 8-9.9 years, and 10-11.9 years.

Each of the 159 children was allocated to only one age group, to provide cross-sectional data on visual acuity development, and allocations were made without reference to visual acuity scores, and so that an approximately even distribution of participants numbers resulted across the age groups. When a child had been seen on more than one occasion within a designated age group, the visit which was closest to the centre of the age range was chosen (e.g. the centre of the 2-3.9 year age group was 34.5 months).

Seven optometrists have been involved in the study over the years, and all contributed some of the data used in this analysis. All were highly experienced at examining children with Down's syndrome.

Visual acuity was measured on each occasion by age and ability-appropriate tests, and thus varied among the participants even within one age group. The tests used were, however, limited to the following, which all have LogMAR-based acuity scales and for which norms are available:

Teller Acuity Cards(12), Cardiff Acuity Test(13), Kay Pictures LogMAR (singles or crowded)(14), Keeler LogMAR Crowded test (formerly Glasgow Acuity Cards – only the crowded version was used)(15).

Binocular acuity was available for all children in the final database, and the norms derived for binocular acuity. Monocular acuity was measured if the child could tolerate both occlusion and repeated measurements, which was relatively infrequent. If the child had spectacles for a distance refractive error, acuity was ‘corrected acuity’ with current spectacles. If a change of refractive error was found during an examination, ‘best corrected’ acuity was rarely recorded with the trial frame, since the unfamiliar experience, discomfort of the trial frame and further repeat of the measurement was unlikely to be tolerated. If no spectacles had been prescribed, then acuity was obviously ‘uncorrected acuity’.

In line with common clinical practice, spectacle prescriptions were not issued for infants. The youngest child with corrected acuity was 12.9 months old. In general, because accommodation is known to be poor in the majority of children with Down’s syndrome(16, 17), our protocol is to prescribe for hypermetropia whenever uncorrected accommodation at near is poor (outside the normal lag)(18, 19); this often means prescribing for lower amounts of hypermetropia than the protocols adopted by many clinics and prescribing the full amount of hypermetropia. Myopic children are prescribed spectacles when the child begins to take an interest in distance viewing; this is determined in discussion with parents and is usually between the ages of 2 and 3 years. Astigmatism is always incorporated in prescriptions for hypermetropia or myopia. Astigmatism alone (i.e. when the equivalent sphere is emmetropia) is corrected when it is over 2.00DC. Visual acuity is never used as a criterion for spectacle prescription. When children were examined later than our bifocal trial(11), bifocals were prescribed for all children with a persistent accommodative lag (i.e. present on two consecutive visits) with full distance error correction, over the age of 2 years.

## Results

Table 1 shows the numbers of children in each age group, the numbers of children using each available test and the numbers of children wearing spectacle correction for acuity testing. Key: T=Teller cards, C=Cardiff Acuity Test, KC= Kay Pictures crowded, KS=Kay Pictures singles, KL= Keeler Crowded.

| Age group       | 1-5.9 months | 6-11.9 months | 12-17.9 months | 18-23.9 months | 2-3.9 years | 4-5.9 years          | 6-7.9 years          | 8-9.9 years                 | 10-11.9 years       |
|-----------------|--------------|---------------|----------------|----------------|-------------|----------------------|----------------------|-----------------------------|---------------------|
| No. of children | 17           | 18            | 16             | 16             | 16          | 20                   | 21                   | 16                          | 19                  |
| No. using tests | 17 T         | 16 T<br>2 C   | 8 T<br>8 C     | 5 T<br>11 C    | 5 T<br>11 C | 15 C<br>4 KC<br>1 KS | 10 C<br>9 KC<br>2 KL | 6 C<br>8 KC<br>1 KS<br>1 KL | 6 C<br>9 KC<br>4 KL |
| No. wearing Rx  | 0            | 0             | 1              | 2              | 5           | 10                   | 12                   | 12                          | 12                  |

Binocular acuity data were not normally distributed for one of the age groups ( 2-3.9 years, Shapiro-Wilk,  $p < 0.04$ ), but since the remaining age groups had normally distributed data, it was decided to use means and confidence intervals in Figure 1, which shows the binocular acuity values for each group, in line with published normal values for typically developing children.

Figure 1 here

Table 2 shows the binocular acuity norms that eye care practitioners can expect in children with Down's syndrome without significant uncorrected refractive error.

| Age group                                    | 1-5.9 months | 6-11.9 months | 12-17.9 months | 18-23.9 months | 2-3.9 years   | 4-5.9 years   | 6-7.9 years  | 8-9.9 years   | 10-11.9 years |
|--|--------------|---------------|----------------|----------------|---------------|---------------|--------------|---------------|---------------|
| Mean binocular acuity (LogMAR)               | 1.15         | 0.81          | 0.67           | 0.5            | 0.37          | 0.28          | 0.28         | 0.18          | 0.25          |
| Range (95% confidence interval)              | 0.75 to 1.54 | 0.51 to 0.10  | 0.18 to 1.16   | 0.14 to 0.85   | -0.01 to 0.74 | -0.04 to 0.59 | 0.08 to 0.49 | -0.12 to 0.47 | -0.01 to 0.50 |
| Proportion failing vision screening criteria |              |               |                |                |               | 11/20<br>55%  | 12/21<br>57% | 5/16<br>31%   | 8/19<br>42%   |

Although the normal range expressed in Figure 1 and Table 2 suggests that acuities as good as -0.12 can be scored for children with Down's syndrome, in practice **this may not be** achieved. Among the cross-sectional data presented here, only five children achieved LogMAR 0.0 acuity binocularly; one was aged 4-5.9 years, three were aged 8-9.9 years and one was aged 10-11.9 years; no child achieved better than 0.0 LogMAR. **In the UK, the national guidelines for vision screening of 4-5 year olds specify the pass criteria of LogMAR 0.2 (monocular acuity; since binocular acuity is usually slightly better than monocular, applying the criteria to this current data would be expected to maximise pass rates). Applying this criterion to children with Down's syndrome in the over 4 years age groups, as Table 2 shows, means that a total of 46% of children would fail standard vision screening.**

Acuity may vary considerably with the test used. **In particular, the pooling of data recorded by preferential looking with data from optotype tests in establishing norms may be questioned. To test this, all binocular acuities were categorised as PL (Teller or Cardiff) or optotype (Kay Pictures or Keeler letters) and an analysis of co-variance was carried out, with age as the covariate. There was no significant difference between acuities recorded by PL and by optotype when age was taken into account ( $F=1.17$ ,  $p=0.28$ ). Since at the older ages, some children were still dependent on preferential looking, combining the test scores to give a single norm is justified.**

**Another confounding factor in the study is the different recruitment sources, and in particular the likelihood of self-selection bias when parents elected to join the study. An analysis of co-variance was again used to determine any effect of recruitment source, define as 'early' or 'late' on the binocular acuity score, with age as the covariate. There was no significant difference between acuities recorded from the early or late recruits, when age was taken into account ( $F=0.01$ ,  $p=0.90$ )**

Nine children were identified who had data for at least 8 of the 9 age groups, which therefore allowed longitudinal analysis of binocular acuity and this is shown for the individuals in Figure 2. Each child shows a progression of acuity in keeping with the cross-sectional data. Note that no acuity score is better than LogMAR 0.0.



Figure 2 here.

Monocular acuity was available for 69 children without strabismus, with ages ranging from 3.9 months to 11.6 years. Mean interocular acuity difference was calculated, using the absolute difference between right and left eyes. The mean interocular acuity difference was LogMAR 0.06 ( $\pm 0.12$ ) and was not influenced by age ( $r=0.22$ ,  $p=0.86$ ) or by test type (preferential looking v. optotype,  $t=0.26$ ,  $p=0.80$ ). The differences between better-eye and binocular acuity (i.e. binocular summation) was available for 64 children, and mean difference was LogMAR 0.06 ( $\pm 0.07$ ) and was not influenced by age ( $r=0.16$ ,  $p=0.2$ ) or by test type ( $t=0.26$ ,  $p=0.80$ ).

## Discussion

This retrospective analysis confirms the previous reports of poor acuity in children with Down's syndrome, even when refractive errors are corrected, at all but the youngest ages. Courage and Adams(1) used the Teller Acuity Cards to record acuity for participants with Down's syndrome from 2 months of age, and noted a deviation from published norms after 6 months of age. Woodhouse et al(3) used Teller Acuity Cards for younger children and Cardiff Acuity Test for older children both with and without Down's syndrome aged 3 to 57 months and showed poorer acuity in Down's syndrome after 24 months. The current analysis (see Figure 1) also suggests a deviation from the expected norms between 3-4 years such that almost half of all children with Down's syndrome over the age of 4 years would fail standard vision screening.

A recent longitudinal evaluation by Tomita(2) suggested that development of visual acuity is delayed rather than abnormal in Down's syndrome, since 50% achieved 0.0 LogMAR by 3 years and 100% by 6 years. However, the authors presented no comparative data from typically developing children, and used non-standardised test procedures. Whether the pictures or Landolt C tests used for 3-6 year olds were presented singly or crowded and whether LogMAR scales were incorporated was not stated.

The current analysis of both cross-sectional and longitudinal data suggests that acuity lies within the typical norms for infants, when preferential-looking tests are used exclusively, but the rate of acuity improvement separates from that of typically developing children from about 3-4 years, and there appears little further acuity development beyond 5 years. Of course a limitation of the current analysis is the use of different tests for acuity; theoretically, preferential looking and optotype tests measure different aspects of vision. In clinical settings, ability appropriate tests must be used; it is clear that a poor score would result from the use of too complex a test for a child and similarly, the use of too simple a test could mean loss of interest in a child subject. In general, children with Down's syndrome would be expected to use a simpler test for age than typically developing children, and in this analysis, we report that a proportion of children were still reliant on preferential looking (the Cardiff Acuity Test) beyond the age of 4 years, when typically developing children would be expected to have progressed to Kay Pictures or letter tests. There is evidence that preferential looking tests over-estimate acuity and are less sensitive to refractive errors and amblyopia (20, 21) in typically developing children, although our analysis showed no difference in scores between children using the preferential looking and optotype tests. The purpose of this analysis is the development of norms for clinical purposes, and we find no difference between the type of test used. This suggests that choosing the test to suit a child's ability is entirely appropriate and the norms can be considered equivalent. Further, the use of simpler tests in children with Down's syndrome could be expected to

minimise any differences in acuity. Instead, the mean values for binocular acuity in children with Down's syndrome are 0.1 to 0.4 LogMAR poorer than typically developing children from the age of 4 years.

In our study, 'best corrected' acuity was not measured, since trial frames were not used for acuity. However, none of the published norms use best corrected acuity and one (norms for Kay Pictures LogMAR (9)) did not measure refractive errors at all in the subject group; uncorrected refractive errors could be a confounder in their data. The study is included here simply because it provides norms for an age group not otherwise represented with the Kay Pictures test. Even with the potential for uncorrected refractive errors, the acuity scored for typical children is, on average, 0.2 better than for children with Down's syndrome.

Accommodative deficits are common among children with DS(16, 17, 22), and our group now corrects such defects with bifocals (11). However, children whose visits were in the early years of our studies would not have bifocals. The presence of a bifocal segment or an accommodative lag would not be expected to influence acuity measures with Kay Pictures or Keeler LogMAR tests, which are conducted at 3 metres. Preferential looking tests (Teller Cards and Cardiff Acuity Test) are conducted at closer working distances and could be influenced by an uncorrected accommodative deficit. However, the norms for Down's syndrome match the norms for typical children when children are very young and entirely dependent on preferential looking. The ages at which a significant proportion of children are using tests at 3 metres, are the ages at which acuities in Down's syndrome are poorer than acuities for typical children.

Little et al (5) assessed acuity in children with Down's syndrome and typical children by conventional grating targets and by interferometric generated grating targets, which eliminated the optical quality of the eyes. Both tasks required the children to identify whether the stripes were horizontal or vertical and were as closely matched as possible for cognitive demand. Acuity for children with Down's syndrome improved for interferometric targets by a factor of FOUR compared to typical children, although acuities were still significantly poorer in Down's syndrome. Since the tasks were the same, this suggests that the poor acuity for conventional targets was not due to behavioural issues. Similarly, the poor acuity demonstrated in the current study is unlikely to be behavioural in nature.

Binocular summation and interocular acuity difference values are available for typically-developing children, for some of the tests used here. Binocular summation for Teller Acuity Cards (estimated from the published data(8)) is up to 0.07 LogMAR, and for Cardiff Acuity Test(6) up to 0.3 LogMAR. For children with Down's syndrome, we found a mean value of 0.06 across all test types. Interocular acuity differences are reported to be up to 0.15 LogMAR for Teller Acuity Cards(8), up to 0.1 LogMAR for Cardiff Acuity Test(6), up to 0.15 LogMAR for Kay Pictures Crowded(9) and, on average, 0.03 LogMAR for Keeler LogMAR Crowded test(10). We found a mean interocular acuity difference of 0.06 LogMAR across all test types. Thus for children with Down's syndrome these aspects would appear to be within the expected range, suggesting that acuity measurements are reliable in children with Down's syndrome but the absolute level of visual acuity can be expected to be poorer than for typical children.

The availability of 'normal' values as produced here, will allow eye care practitioners to reassure parents when their child's vision is within the expected range for Down's syndrome. However, visual acuity is poorer than expected when compared to typically developing children. Studies suggest that contrast sensitivity too is reduced in children with Down's syndrome(4, 23). It is, therefore, imperative that practitioners explain to parents and to teachers that a child's vision is below normal

when compared to classroom peers. Children with Down's syndrome are considered to be visual learners(24), that is, they are more reliant on vision for learning than are typically-developing children. It could be argued then, that reduced vision is more detrimental to learning in a child with Down's syndrome, than it is in a typically-developing child, who can compensate for vision loss by making use of their auditory and cognitive skills. Teachers need to be aware that the child in their classroom who has Down's syndrome is not seeing their school work as readily as the other children. If the teacher is not aware that a child's vision is poor, then inability to carry out tasks in the classroom may be considered to be due to the learning disability and nothing done to address the issue. Simple enlargement of learning material may be all that is needed. Eye care practitioners have a responsibility to keep parents and teachers fully informed of a child's visual development, *in comparison to typical children*, as well as with reference to the expected values for Down's syndrome, **in order that everyone associated with a child can understand their capabilities and what needs to be done to support their learning.**

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Figure 1. Mean binocular visual acuities (filled markers and continuous lines) and 95% confidence limits (open markers and dotted lines) for children with Down's syndrome, using a variety of tests, alongside the published norms (means and 95% confidence limits) for the same range of tests, i.e. Teller Acuity Cards(8), Cardiff Acuity Test(6), Kay Pictures Crowded(7, 9) and Keeler LogMAR Crowded(10). Note that norms for Teller Cards and Cardiff Acuity Test are for binocular measures, while norms for optotype tests are for monocular assessment.

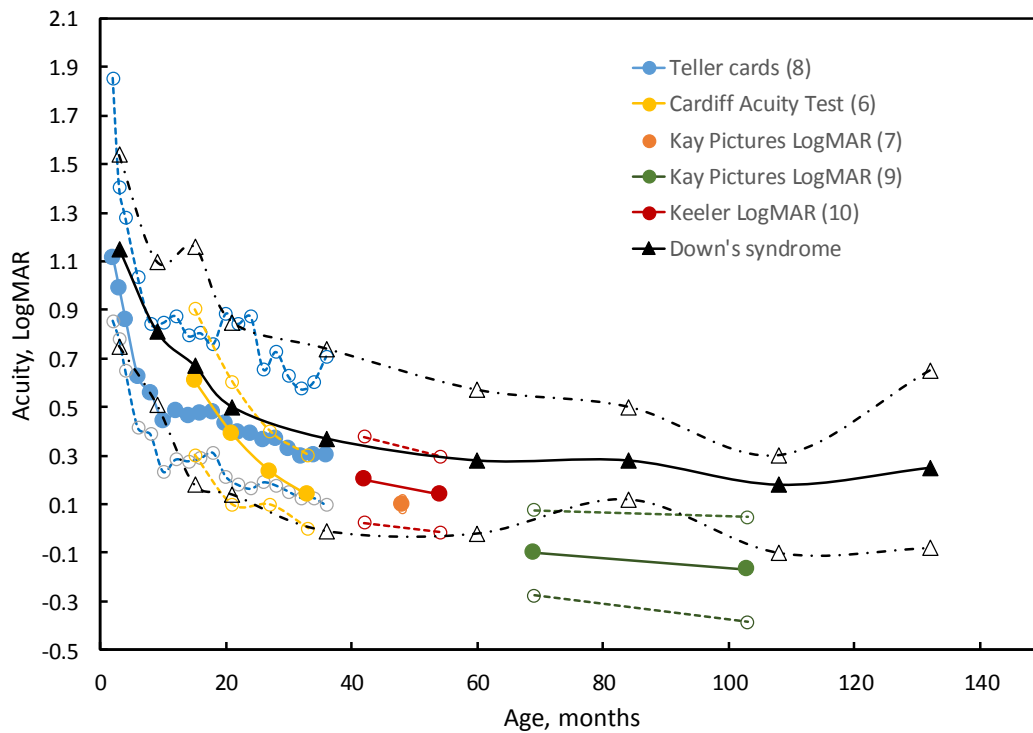


Figure 2. Mean binocular acuity values **for individual** children with Down's syndrome followed longitudinally, in comparison with the cross-sectional data (mean and 95% confidence limits) from Figure 1. Note that each child in the longitudinal data set contributes only ONE data point to the cross-sectional values.

