Introduction

Strabismus is a common ocular manifestation of Down syndrome; incidence figures range between 19% and 42% (Haugen & Hovding 2001; Cregg et al. 2003; Yurdakul et al. 2006; Ljubic et al. 2011; Ljubic et al. 2015), compared to the 2%–5% incidence in the general population (Robaei et al. 2006; Friedman et al. 2009). Of those with strabismus, 71%–100% (Haugen & Hovding 2001; Cregg et al. 2003; Yurdakul et al. 2006; Ljubic et al. 2011; Ljubic et al. 2015) are reported to have esotropia, although the specific types of esotropia are not stated. Similarly, it has also been reported that incidence of strabismus is increased in children with developmental delay, with figures ranging from 17.4–40.0% (Bankes 1974; Nielsen et al. 2007; Das et al. 2010). Again, a trend towards esotropia has been reported, although in the developmental delay population figures for esotropia range between 14.9% and 76.8% of strabismus cases, suggesting more variability in this population.

While the increased prevalence of strabismus is known, the aetiology of the strabismus in both populations is not fully understood. However, within the Down syndrome population it is well documented that in combination with the increased rates of strabismus, the incidence of hypermetropia is also increased. Although the increased rates of hypermetropia may be a significant factor resulting in the increased rates of strabismus, Cregg et al. (2003) reported a lack of a statistical association between strabismus and hypermetropia in their longitudinal study (p = 0.539, n = 55, representing approximately just 0.14% of the UK population of individuals with Down syndrome). Given the lack of association, it was theorised that an aspect of the aetiology may be a result of hypotonic extracocular muscles, congruous in the context of the generalised hypotonia of individuals with Down syndrome (Corrêa et al. 2011). Considering that the manifest strabismus
may not be corrected with spectacle lenses, individuals may wish to consider strabismus surgery to improve their ocular alignment.

This paper aims to review existing reports regarding techniques and amounts of surgery, in order to establish whether surgical doses should be adapted for individuals with Down syndrome. The available literature has often included individuals with Down syndrome in cohorts studied under the term of developmental delay. Developmental delay is an umbrella term for children experiencing delay in two or more areas of development categories: fine/gross motor skills, speech and language development, cognition, social/personal, and activities of daily living (Majnemer & Shevell 1995; Shevell et al. 2003; Mithyantha et al. 2017). Developmental delay may occur alone, or alongside another condition. As the term covers children with a wide range of developmental abilities it can be open to interpretation; for example, individual states in the US have their own definition of developmental delay, and differing age ranges to which the diagnosis applies (Hadadian & Koch 2013). Due to this scope in definition, literature available has often studied cohorts with a variety of conditions, including Down syndrome, under the term ‘developmental delay’. As a result, the scope of this review will also cover individuals described as having developmental delay, whilst focusing on the cohort with Down syndrome. In addition, this review and the literature covered will primarily consider the surgical effect on esotropia due to the high incidence of esotropia in the populations studied.

Methods

The starting point for this literature review was the article by Pickering et al (1994). Working from this point, a citation search was performed using Web of Science, returning 26 citations. Articles considering strabismus surgery in individuals with Down syndrome or developmental delay were selected for inclusion (total n = 7, including the original Pickering et al 1994 article). Articles pertaining to strabismus surgery in individuals with cerebral palsy, prematurity and infantile esotropia, as identified in the title of the article, were excluded due to the effect of these diagnoses on surgical outcomes requiring separate analysis. Articles written in any language other than English (n = 1) were excluded. One review article (Liu & Ranka 2014) was not selected for inclusion to avoid possibly including bias from secondary interpretation; however, the references were used to find further original research articles for inclusion (total for inclusion n = 10).

Searches of PubMed using the terms ‘strabismus’, ‘developmental’, and ‘delay’, as well as ‘strabismus’, ‘down’, and ‘syndrome’ returned 280 and 157 results respectively. Articles relevant to this literature review, as established by their title, but not identified using searches described previously, were selected using the above criteria, with one further article selected for inclusion (total articles included n = 11).

Results

Table 1 summarises the studies examining surgical effect in populations under the heading developmental delay and in populations with Down Syndrome.

Informed Discussion

Pickering et al (1994) were among the first to investigate surgical response in children that had developmental delay. They advocated a reduced surgical dose for children with developmental delay, after retrospectively analysing the surgical outcomes of 31 children with developmental delay and 63 typically developing children. Of the children with developmental delay, 17 were classified as having neurological conditions such as cerebral palsy, hydrocephalus and seizures, six had chromosomal abnormalities, including Down syndrome, whilst the remaining eight patients had non-specific developmental delay. The authors had anecdotally noted a trend towards overcorrection in the developmental delay population. Comparison of outcomes between children with developmental delay and typically developing children undergoing bilateral medial rectus recessions between 1981 and 1991, demonstrated that the children with developmental delay experienced on ‘average’ (presumably mean, but not specified and no standard deviation given) an extra 5.28 prism dioptres in surgical correction towards exotropia. However, while this difference between the two groups was statistically significant at one month postoperatively (p = 0.04), the difference was not significant at one year postoperatively (p = 0.08). For children receiving 4.0 mm recessions of each medial rectus the surgical effect was in fact greater towards exotropia in the typically developing children than in the developmentally delayed children, at both one month and one year postoperatively, although this data point was not individually analysed for statistical significance. While the authors concluded that their findings supported reducing the surgical dose for individuals with developmental delay, this conclusion is not supported by their data.

In a follow up study a year later, Pickering et al (1995) examined how performing reduced amounts of surgery on children with developmental delay impacted on the outcome of their surgery. Success was defined as alignment within 10 prism dioptres of orthophoria. Statistical analysis was not significant when comparing the outcomes between the two groups when they received the same amount of surgery (p = 0.20, total participants across both groups n = 91), and when the surgical dose was altered in the developmental delay group (p = 0.70, n = 29). Despite statistically insignificant results Pickering et al (1995) advocated performing reduced bimedial rectus recessions in children with developmental delay. No specific reduction was suggested; however, the authors reported that they reduced their surgeries by an average of 0.54 mm, with no standard deviation given.

Based on the work by Pickering et al (1994, 1995), some surgeons opted to reduce their bimedial recession in patients with developmental delay. Habot-Wilner et al (2006) used reduced surgical doses, retrospectively reviewing case notes of 34 children: 16 with developmental delay, of whom two had a diagnosis of Down syndrome, and 18 typically developing controls that underwent bimedial rectus recession between 1993 and 2003. Those in the developmental delay group were given a deliberately reduced surgical dose, by a mean of 0.84 mm per muscle.
| Authors                     | Study Design       | Participants                                                                 | Age                      | Strabismus            | Surgery       | Surgical Adjustment                                                                 | Outcome (success = within 10° of orthotropia) |
|-----------------------------|--------------------|------------------------------------------------------------------------------|--------------------------|-----------------------|---------------|--------------------------------------------------------------------------------------|-----------------------------------------------|
| Pickering et al (1994)      | Retrospective      | N = 94                                                                       | Mean 25 months (range 10–80 months) | Esotropia 49°, range 25°–70° DD group | BMRR          | “less surgical correction” performed for “some” children in DD group                  | 69% success at 1 month post op DD group       |
|                             | Review             |                                                                             |                          |                       |               |                                                                                     |                                               |
|                             |                    | 31 DD group 23 known diagnosed condition                                      |                          |                       |               |                                                                                     |                                               |
|                             |                    | 63 typically developing controls (TD)                                         |                          |                       |               |                                                                                     |                                               |
|                             |                    | Mean 26 months (range 7–202 months)                                          | 50°, range 18°–95° TD group |                       |               | No adjustment given to TD group                                                      | 82% success at 1 month post op TD group      |
|                             |                    |                                                                             |                          |                       |               |                                                                                     |                                               |
|                             |                    | 62 TD controls                                                               | Mean 26 months (range 7–202 months) |                       | BMRR          | “less surgery” given to children in DD group after 1987 average 0.54 mm per muscle | DD pre-1987 76% success DD post-1987 86% success (no n number given) |
|                             |                    |                                                                             |                          |                       |               |                                                                                     |                                               |
| Habo-Wilner et al (2006)    | Retrospective      | N = 34                                                                       | 3.7 ± 2.7 yrs            | Esotropia 53 ± 12° in DD group | BMRR          | 40°–40° reduced by 1 mm per muscle 25°–35° reduced by 0.5 mm per muscle             | 56% (n = 9) within 10° of orthotropia. 86% of surgical failures under corrected in DD group |
|                             | Review             |                                                                             |                          |                       |               |                                                                                     |                                               |
|                             |                    | 16 DD group 8 known diagnosed condition                                       |                          |                       |               |                                                                                     |                                               |
|                             |                    | 18 TD controls                                                               | 37.4 ± 8° in TD group    |                       |               | No adjustment given to TD group                                                      | 94% (n = 17) success in TD group             |
|                             |                    |                                                                             |                          |                       |               |                                                                                     |                                               |
| van Rijn et al (2009)       | Retrospective      | N = 104                                                                      | 69.3 ± 41.3 months       | Esotropia Angle at 2.5 m 16.6 ± 7.2 | 11 single recession | Study group given “roughly halved” doses for single recessions and BMRR after June 2004 | Pre-June 2004 average angle at 2/12 f/up −4.09 ± 6.44° (n = 11). Post June 2004 average angle at 2/12 f/up +1.25 ± 4.14° (n = 16) (p = 0.028) |
|                             | Review             |                                                                             |                          |                       | 16 BMRR       |                                                                                     |                                               |
|                             |                    |                                                                             |                          |                       | 10 R + R      |                                                                                     |                                               |
|                             |                    | 67 TD controls                                                               | 59.2 ± 31.5 months       | Angle at 2.5 m 14.4 ± 7.7 | 16 single recession | No adjustment given to TD group                                                      |                                               |
|                             |                    |                                                                             |                          |                       | 27 BMRR       |                                                                                     |                                               |
|                             |                    |                                                                             |                          |                       | 24 R + R      |                                                                                     |                                               |
| Habo-Wilner et al (2012)    | Retrospective      | N = 24 (some previously included in 2006 study) 9 known diagnosed condition | 2.8 ± 2.5 yrs, (range 0.8–10 yrs) | Esotropia 49.8° ± 13.3° | BMRR          | Mean dose of 5.1 mm ± 0.7 mm per muscle (authors report an average of 0.75 mm less than standard) | 38% (n = 9) success. 67% of surgical failures (n = 10) under corrected |
|                             | Review             |                                                                             |                          |                       |               |                                                                                     |                                               |
|                             |                    | 15 non-specific delay                                                        |                          |                       |               |                                                                                     |                                               |

(Contd.)
| Authors              | Study Design | Participants   | Age             | Strabismus       | Surgery     | Surgical Adjustment                                                                 | Outcome (success = within 10° of orthotropia) |
|---------------------|--------------|----------------|-----------------|------------------|-------------|-------------------------------------------------------------------------------------|---------------------------------------------|
| Swaminathan et al (2014) | Retrospective Review | N = 78          | 4.96 ± 3.25 yrs | Esotropia        | BMRR        | Greater surgical under-correction planned for DD group                              | 60% (n = 15) success, 28% (n = 7) under corrected in DD group |
|                     |              | 25 DD group     |                 |                  |             |                                                                                     |                                              |
|                     |              | 10 known diagnosed condition |             |                  |             |                                                                                     |                                              |
|                     |              | 53 TD controls  |                 |                  |             |                                                                                     |                                              |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |
| Zehavi-Dorin et al (2016) | Retrospective Review | N = 42          | Mean 2.9 yrs (range 0.8–10yrs) | Esotropia        | BMRR        | Mean dose of 0.66 m (range 0–1. mm) less than surgical tables                        | 74% (n = 39) success, 26% (n = 14) under corrected in TD group |
|                     |              | 17 known diagnosed condition |             |                  |             |                                                                                     |                                              |
|                     |              | 25 non-specific delay |             |                  |             |                                                                                     |                                              |
|                     |              | 53 TD controls  |                 |                  |             |                                                                                     |                                              |
| Ruttum et al (2004) | Retrospective Review | N = 21 DS      | Mean 55 (±35) months | Esotropia        | BMRR        | None–surgical methodology not discussed further                                      | 67% (n = 14) within 10° of orthotropia       |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |
| Yahalom et al (2010)  | Retrospective Review | N = 15 DS (14 outcomes analysed) | Mean 6.2 yrs (range 1.2–24.9 yrs) | Esotropia        | BMRR        | Standard surgical tables used.                                                      | 86% (n = 12) within 10° of orthotropia      |
|                     |              | 14x infantile esotropia |                 |                  |             |                                                                                     |                                              |
|                     |              | 1x constant esotropia with an accommodative element | |                  |             |                                                                                     |                                              |
|                     |              | 12x BMRR 2x R+R 2x unknown |             |                  |             |                                                                                     |                                              |
| Perez et al (2013)  | Retrospective Review | N = 17 DS      | Mean 5.9 (±3.8) yrs | 10x infantile esotropia | BMRR        | Standard surgical tables used in both groups                                       | 76% (n = 13) within 10° of orthotropia      |
|                     |              | 7x acquired esotropia |             |                  |             |                                                                                     |                                              |
| Motley et al (2012)  | Retrospective Review | N = 16 DS      | Median 4.1 (IQR 3.2–6.8) yrs | Esotropia        | BMRR        | Standard surgical tables used in both groups                                       | 85% (n = 23) within 10° of orthotropia      |
|                     |              | 14x acquired esotropia |             |                  |             |                                                                                     |                                              |
|                     |              | 14x constant esotropia with an accommodative element | |                  |             |                                                                                     |                                              |
|                     |              | 3x R+R          |                 |                  |             |                                                                                     |                                              |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |
| Motley et al (2012)  | Case Control  | N = 27 Matched controls | Mean 5.1 (±2.8) yrs | 14x acquired esotropia | BMRR        | Standard surgical tables used in both groups                                       | 85% (n = 23) within 10° of orthotropia      |
|                     |              | 14x constant esotropia with an accommodative element | |                  |             |                                                                                     |                                              |
|                     |              |                  |                 |                  |             |                                                                                     |                                              |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |
| Motley et al (2012)  | Case Control  | N = 16 Matched controls | Median 4.6 (IQR 3.5–5.9) yrs | Esotropia        | BMRR        | Standard surgical tables used in both groups                                       | No statistical difference in outcome between groups. Success rates not given (P = 0.850) |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |
|                     |              |                 |                 |                  |             |                                                                                     |                                              |

DS – Down Syndrome.
TD – Typically Developing.
BMRR – Bilateral Medial Rectus Recessions.
R+R – Medial Rectus Recession with Lateral Rectus Resection.
^ – Prism Dioptres.
Harrison et al: Strabismus Surgery for Esotropia, Down Syndrome and Developmental Delay; Is an Altered Surgical Dose Required? A Literature Review

The difference in outcomes between the typically developing individuals as purported by Pickering et al (1994, 1995). The difference in outcomes between the developmentally delayed population from this work as the reductions of 0.84 mm per muscle performed are greater than those suggested by Pickering et al (1995). Therefore, whilst the results of Habot-Wilner et al (2006) do not support reductions of 0.84 mm per muscle, they cannot dismiss the possibility that smaller surgical reductions may lead to improved outcomes in patients with developmental delay.

Expressing the Surgical Dose

It can be helpful to consider the surgical dose expressed as a percentage correction of the strabismic angle (using surgical tables), rather than in millimetres of muscle adjustment, to understand the impact of alteration of the surgical dose (Swaminathan et al. 2014). Swaminathan (2014) reported on a case control study of 25 children with developmental delay (excluding Down syndrome) and 53 typically developing controls, described as having concomitant esotropia. The authors calculated expected surgical effect for the bimedial rectus recessions per muscle performed are greater than those suggested by Pickering et al (1995). Therefore, whilst the results of Habot-Wilner et al (2006) do not support reductions of 0.84 mm per muscle, they cannot dismiss the possibility that smaller surgical reductions may lead to improved outcomes in patients with developmental delay.

The results of Habot-Wilner et al (2006) demonstrated that a reduction of surgery by an average of 0.84 mm per muscle in the developmentally delayed population resulted in a statistically significant increase in surgical failure (undercorrection of >10 prism diopters), compared with the typically developing group receiving standard surgery. Despite this statistically significant result, the authors concluded that the ideal surgery for the developmentally delayed population could not be defined, due to the majority of children in both study groups only being followed up for one year. It is also difficult to determine an ideal amount of surgery in the developmentally delayed population from this work as the reductions of 0.84 mm per muscle performed are greater than those suggested by Pickering et al (1995). Therefore, whilst the results of Habot-Wilner et al (2006) do not support reductions of 0.84 mm per muscle, they cannot dismiss the possibility that smaller surgical reductions may lead to improved outcomes in patients with developmental delay.

Long Term Follow Up

In order to try and establish the ideal surgical dose, two follow up studies were undertaken at the same centre (Habot-Wilner et al. 2012; Zehavi-Dorin et al. 2016). Habot-Wilner et al (2012) reported on children meeting their inclusion criteria at their centre between 1993–2009. Their previous study reported on the years 1993–2003, and there is therefore some overlap between the two works. In this follow up study the average surgical reduction was 0.75 mm per muscle, range 0–1.5 mm (previously average 0.84 mm reduction per muscle). After one surgery success rates were still poor at 38% (n = 9) with 42% (n = 10) under corrected and 21% (n = 5) overcorrected. Eight of the 15 surgical failures opted for further surgery, with seven children receiving one additional surgery, and one child receiving two additional surgeries. The overall success rate after all additional surgeries was 61% (n = 24). Although this follow up study reported lower surgical success rates with smaller surgical reductions, other authors from the same centre reported conflicting results.

Zehavi-Dorin et al (2016) reviewed surgical outcomes of 42 children with developmental delay, of whom four had Down syndrome and 13 had another specific diagnosis. The children underwent bilateral medial rectus recession, on average reduced by 0.66 mm from the standard dose (range 0–1.5 mm) and were followed up for median 3.67 years (range 8 months to 15 years). This resulted in a surgical success rate of 57% (n = 24), defined as heterotropia of less than 10 prism diopters, with 31% (n = 13) under corrected and 12% (n = 5) overcorrected, congruent with the 60% success and 12% overcorrection rates reported by Swaminathan et al (2014) in their developmental delay population. These success rates are greater than those reported by Habot-Wilner in their original and follow up studies, where their data had appeared to show lower surgical success rates, with smaller surgical reductions.

Zehavi-Dorin et al (2016) also examined the longer-term data available for 16 children who had been followed up for five years, finding that after five years surgical success was 43% (n = 7), with 37.5% (n = 6) undercorrected and 18.5% (n = 3) overcorrected. This could suggest a longer-term trend towards overcorrection in the developmental
delay population, and support an argument for initial under correction for longer term success to account for post-operative drift (Park et al. 2009).

Type of Surgery
Whilst both Pickering et al (1994, 1995) and Habot-Wilner et al (2006) only examined the surgical effect of bimedial rectus recessions in the developmentally delayed population, van Rijn et al. (2009) studied both bimedial rectus recessions and unilateral recess/resect procedures. van Rijn et al (2009) reported that whilst there was no significant difference in the outcomes of developmentally delayed children (including four with Down syndrome) compared to typically developing children undergoing unilateral recess/resect procedures ($p = 0.918$ at 30 cm fixation distance), there was a significant difference between the two groups for those undergoing bimedial rectus recessions ($p < 0.001$ at 30 cm fixation). The deviations were however measured deviations using a Maddox method. This was a custom-made device chosen by the authors to avoid the possibility of inducing proximal vergence by using prisms, although no published evidence to support their argument has been found. Typically, Maddox methods still require a rod or wing device to be placed in front of the eye, also inducing proximal vergence and therefore negating the authors reasoning. The methodology described measuring deviations fixing both right and left eye and did not report any alternative measurement process. Given that the authors studied children with developmental delay, some of whom were as young as 18 months old, it is difficult to be confident that subjective measurements have given accurate results to analyse. It could however be postulated that as the methodologies between the two groups are the same, this does not impact on the authors’ conclusions, it simply prevents replication.

van Rijn et al (2009) were unable to explain the causation for the difference in outcomes between the surgeries, but theorised that the difference was due to the balance between the tone of the lateral and medial rectus muscles being disturbed by bimedial rectus recessions, but not by unilateral recess/resect procedure. The relevance of this theory for individuals with Down syndrome is difficult to ascertain, given the possibility that the tone of the extra ocular muscles may be altered in individuals with Down syndrome. Individual patients will have different visual development experiences, and therefore limiting the explanation for difference in outcomes only to muscle tone may be artificial. This explanation does not consider the impact of visual acuity, which is also known to be reduced in individuals with Down syndrome (Zahidi et al. 2018), or of the presence or absence of binocular single vision which influence the surgical outcome (Kiziltunc et al. 2016).

Surgical and Strabismus Measurement Technique
When evaluating the surgical outcomes, the accuracy of the measurements must be considered, both of the surgical measurements and of the measurement of strabismus. Castroviejo callipers used in strabismus surgery mark only to the whole millimetre, and do not have markings for micrometres. It should also be considered that at such small distances, the positioning of the callipers on the sclera, and whether the measurement is taken from the inside or outside edge of the calliper, will have a proportionally greater impact on the accuracy of the measurement than for larger distances. A surgeon could not therefore measure 0.54 mm or 0.84 mm using standard surgical equipment, casting doubt on the validity of the findings and recommendations of Pickering et al (1994) and Habot-Wilner et al (2006).

Strabismus measurement methodology is also pertinent, given that the research explored uses angle of strabismus to define surgical success. Accurate measurement is therefore required in order to reach robust conclusions on surgical success. Several studies discussed herein (Pickering et al. 1994; Pickering et al. 1995; Yahalom et al. 2010) measured deviations using the prism cover test, and the Kirmsky method where this was not possible. Kirmsky methods and alternate prism cover test (APCT) were examined by Joo et al (Joo et al. 2013), reporting statistically significant ($p < 0.001$) intraobserver agreement for standard near Kirmsky, modified distance Kirmsky and APCT methods. When measuring esotropia the Pearson correlation coefficient for near Kirmsky and distance APCT was $0.651$ ($p = 0.003$), and $0.695$ ($p = 0.001$) for distance Kirmsky and distance APCT. These findings would suggest good intraobserver agreement between the tests, and strong positive correlation between distance Kirmsky and distance APCT, with slightly weaker correlation between near Kirmsky and distance APCT.

While Kirmsky and distance APCT may have strong positive correlation, suggesting good agreement between the two measurement methods, a test must also be repeatable. The test-retest variability of the APCT, researched on adults with sixth nerve palsy, and based on 95% confidence intervals has been reported as being 10.2 prism diptres for distance fixation and 9.2 prism diptres for near fixation (Holmes et al. 2008). A measurement difference of 5.28 prism diptres, given as the difference in outcome between the developmentally delayed and typically developing groups in the work by Pickering et al (1995), is easily accounted for by test retest variation, and this difference could therefore be considered clinically insignificant.

Research Exclusively in the Down Syndrome Population
Whilst the research discussed thus far examines the surgical effect of strabismus surgery on groups of participants with development delay, including those with Down syndrome, it is not possible to specifically analyse the outcomes of just the participants with Down syndrome from the published results. Other authors (Motley et al. 2012; Perez et al. 2013; Ruttum et al. 2004; Yahalom et al. 2010), however, studied only participants with Down syndrome. Their findings are summarised in Table 1.

As shown in Table 1, there is some variation in outcomes, and in how the outcomes are measured and reported between studies. Unlike others, Ruttum et al (2004) did
not use a control or comparison group, and did not reduce the surgical dose given; the authors instead compared their success rates to those in the published literature. Their success rate of 67% (n = 14) is higher than the success rates of 56% (n = 16) reported by Habot-Wilner et al (2006) and the 60% (n = 25) success rate reported by Swaminathan et al (2014), both of whom used reduced surgical doses. This could suggest reduced surgical doses may result in a poorer success rate, although the research populations have differing characteristics between these studies.

**Participant Demographics**

Whilst Ruttum et al (2004) achieved higher success rates than Habot-Wilner (2006) with standard surgical dosing, suggesting that the reduced surgical dose has little impact on outcomes, the demographics of the study groups in terms of diagnosis and surgical dosing are different. Participant demographics are also relevant to Yahalom et al (2010), who described 14 of their patients as having infantile esotropia. Studies exclusively studying infantile esotropia were not included within the scope of this literature review as an individual with Down syndrome may be precluded from a diagnosis of infantile esotropia; since infantile esotropia can be considered to occur in the absence of any other neurological abnormality (Louvagie et al. 2009). This type of strabismus in an individual with Down syndrome may alternatively be diagnosed as a non-accommodative esotropia, as done by Habot-Wilner et al (2006). It could, however, be argued that some neurological impairments may cause infantile esotropia, and that the two diagnoses are not mutually exclusive (Costenbader 1961; von Noorden 1988; Charles & Moore 1992; Simonz & Kolling 2011), or that infantile esotropia itself is a neurological disorder (Brodsky 2018). Other authors (Ruttum et al. 2004; Motley et al. 2012) however gave no classification of esotropia in their study group, particularly problematic for Ruttum et al (2004) as they compared their results to two studies, one exclusively concerning infantile esotropia, the other one acquired esotropia. It could be argued that this comparison is invalid since the surgical timing and outcomes are different in different types of strabismus (Christiansen et al. 2008).

**Surgical Success in Individuals with Down Syndrome**

Yahalom et al. (2010) report the highest surgical success rates of all the Down syndrome population studies identified. One child in their series was given a reduced surgical dose as the surgeon was influenced by literature advocating this approach, however this resulted in an unsuccessful surgery outcome of residual esotropia of greater than 10 prism dioptres. The other participants in this series receiving a standard surgical dose do not appear to have shown an exaggerated surgical response. This finding was replicated by Perez et al (2013), who overcame the difficulties of comparing between studies by using control groups to compare surgical outcomes following bimedial recessions between children with Down syndrome and typically developing children. Both groups received standard surgical doses from the same surgeon. The difference between the success rates in the two groups was not statistically significant (p = 0.46, n = 44). Motley et al (2012) also reported no significant difference between surgeries performed on their two matched groups, with no statistically significant difference in outcomes between the two groups over a 24-month follow-up period (p = 0.8050, n = 32). Information on methodology was however extremely limited, with no details given on measurement of strabismus; an important measure to consider when reviewing outcomes, as discussed previously.

In contrast to the conclusions of van Rijn et al (2009), the findings of Yahalom et al (2010), Motley et al (2012) and Perez et al (2013), would suggest that children with Down syndrome do not have an exaggerated response to bimedial recessions. The success rate reported by Yahalom et al (2010) was 86% (n = 12); very similar to the 85% (n = 23) success rate in typically developing children reported by Perez et al (2013) who did not have a statistically significant difference in outcomes between their two groups (p = 0.46). This would suggest agreement in the findings between the two studies, and broadens support for standard strabismus surgery in individuals with Down syndrome.

**Conclusion**

The evidence discussed here has demonstrated that for individuals with Down syndrome there is no clear evidence to support giving a reduced surgical dose, as standard surgery gives outcomes comparable to those of typically developing children receiving standard surgery. Although the cohorts of individuals with Down syndrome in all studies are small, reducing the reliability of individual studies, this finding has been replicated across the studies discussed. While published research is limited to retrospective reviews of esotropia surgery, with the type of esotropia not well classified, and the subclassification not analysed as a variable influencing the success of strabismus surgery, there is no evidence to suggest that the research findings are not applicable to other types of strabismus within the same population. The limitations regarding analysis described above leave the possibility that confounding variables may be influencing results.

Literature studying individuals under the umbrella term of developmental delay would suggest that there may be some populations under this term that could benefit from reduced surgical dosing. The field would benefit from prospective trials involving participants with unifying diagnoses to identify these populations.

**Competing Interests**

The authors have no competing interests to declare.

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