

XYY



Growing up with XYY





13 years



15 years



16 years



17 years

XYY syndrome

Approximately one boy in 1000 has XYY chromosomes. In the cells of their body, instead of 46 chromosomes including one X and one Y chromosome, they have one X and two Y chromosomes, making 47 in all. The impact of the extra Y chromosome is extremely variable.

The great majority of boys and men with an extra Y chromosome are never aware of it, because they do not have symptoms that lead to a diagnosis. Only a small fraction of boys and men with XYY are ever diagnosed: recent estimates suggest 2.5% in the United Kingdom and 20% in Denmark.

Key features

- Normal appearance, typically tall stature
- Intelligence usually in the normal range, but an increased need for educational support especially with reading and writing
- Increased vulnerability to ADHD (attention deficit hyperactivity disorder)
- Increased vulnerability to autistic spectrum disorders
- Perhaps increased risk of asthma and epilepsy

Sources

Recently more than 700 published studies of the outcomes of having an extra sex chromosome were identified (Leggett 2010). This guide draws chiefly on recent key studies, but also on some of the early screening studies. They are as follows:

Screening studies: Walzer 1990; Götz 1999; Ratcliffe 1999

Follow-up studies of babies identified in pregnancy: Linden 2002; Lalatta 2012

Follow-up studies of babies, boys and men diagnosed because of something unusual: Schiavi 1984; Theilgaard 1984

In recent publications, babies identified in pregnancy are studied as well as boys and men identified because of a problem. These studies help to characterize the possible problems in XYY, but can give a misleading impression of how common these problems are: Geerts 2003; Ross 2009; Stochholm 2010; Bishop 2011; Bryant 2012; Cordeiro 2012; Ross 2012; Stochholm 2012; Tartaglia 2012; Bardsley 2013; Lepage 2014.

The boys reported in Bishop 2011 formed a cohort for a study known as Diesc. Outcomes of this study were reported to Unique members, and are referred to here as Diesc 2010. Additional information comes from Unique families. When this guide was written, Unique had 290 XYY members. In 2003, 43 members completed a survey, and in 2014, 46 families or young men with XYY completed a survey.

How do we know about XYY?

If most boys and men with XYY are never diagnosed, how do we know about the impact of the extra Y chromosome?

Published studies examine different groups of boys and men with XYY:

- Screening studies of newborn babies in which babies found to have XYY were followed up into adulthood
- Follow-up studies of babies identified coincidentally during pregnancy
- Follow-up studies of babies, boys and men diagnosed because of a problem, most often with speech or behaviour.



The first two types of study are very helpful in suggesting how likely it is that a boy will have any problems due to the extra chromosome, or will need any special treatment or support. They show that not all boys do encounter problems. These studies are also helpful in describing some of these problems.

The third type of study focuses on the severe end of the spectrum of XYY, boys and men diagnosed because they have a problem. This type of study is helpful in characterising what the problems are. Recently, studies have also started to look at effective treatments, and at the genes on the Y chromosome that may underlie any problems.

Causes

Boys with XYY chromosomes have an additional Y chromosome from their father. In the great majority of cases, if not all, the two Y chromosomes fail to separate when sperm cells are formed. During this process a cell must first replicate its chromosomes so that it has two copies of each and then divide twice to produce four sperm cells. In some cases both of the Y chromosomes will go to the same cell and when this fertilises an egg (when a baby is made) will produce an embryo with two Ys. It is also possible that a similar event could occur in the very early stages of the development of an embryo.

Main physical features

Height: tall

Boys and men with XYY are often but not always taller than their peers. It is common for them to reach 6'3" (1.88m) and taller. There is some uncertainty about when the extra height becomes apparent, but two recent studies including a total of 134 boys and men both found that height was normal until approximately 6 years of age and then began to increase; at 11 years almost all boys were taller than average and at 13 nearly all the boys were significantly taller than their peers. Most boys over 6 years were in the tallest 15% of boys for their age and most over 13 were in the tallest 2%. All of the boys had normal proportions and most were a normal weight for their height, although some boys in a recent American study showed a tendency towards overweight around the midriff (central adiposity) (Ratcliffe 1990; Geerts 2003; Ottesen 2010; Bardsley 2013).

A survey of Unique families gave a slightly different picture. Among 26 families who told Unique when their son's exceptional length or height was first noticed, eight remarked on it at birth or in babyhood, seven noticed at pre-school, three in the primary school years and in eight boys the extra height was not noticed until puberty. Six out of 19 families with a son below 16 said that his height was not unusual and some boys were small for their age. One family with two six-foot sons remarked that the extra height in the boy with XYY was accounted for in leg length (Unique).

Being tall: advantages and disadvantages

Asked to suggest advantages and disadvantages of the extra height, Unique parents suggested many more disadvantages. These included being picked on as a ringleader; a stooping posture; unfair expectations; size 17 feet; finding shoes and clothes; seating on public transport; being stared at; back weakness and bullying. The chief advantages were for sports such as basketball and as a boost for self esteem. Men with XYY were more accepting of their extra height, only counting as disadvantages hitting their head; buying trousers (pants); and standing out or being picked on in school.

Large head

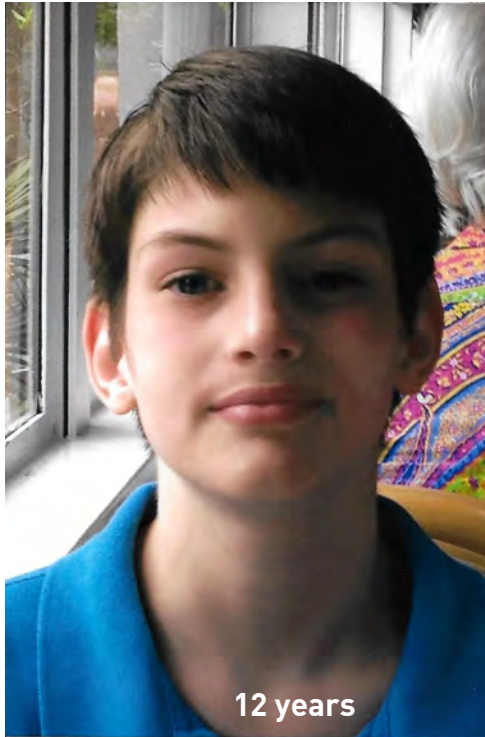
Recent studies have drawn attention to the fact that some boys with XYY have a large head: one in 3, according to a recent study of 90 boys. Older boys were more likely to have a large head than younger boys (Ross 2011; Lalatta 2012; Bardsley 2013). A smaller study including 8 boys with XYY found that their brains were larger than boys with XY chromosomes (Bryant 2012).

Eyes set slightly far apart

Recent studies have drawn attention to the fact that boys' eyes may be set slightly further apart than for boys with XY chromosomes. The bridge of the nose may also be a little broad and the cheek area slightly flat. These are very subtle

features, and not ones that parents would normally notice unless they were drawn to their attention (Lalatta 2012; Bardsley 2013).

“XYY is a difficult disorder to understand as they look very normal.”



Teeth

Boys with XYY are likely to have larger teeth with longer roots than other boys. They can also have a forward-jutting lower jaw and underbite. Dental problems have been found in approximately 1 in 5 boys (20%) (Lähdesmäki 2004; Bardsley 2013).

Unique parents reported some kind of dental problem in a much larger number: 3 boys out of 4 (14/19). The problems include failure of first (milk) teeth to fall out; overcrowded teeth; poor enamel quality; and missing teeth. Some of these dental concerns may not be explained by the extra Y chromosome. Some boys had teeth removed due to overcrowding; others wore braces to correct the dental position.

“Too large for his small mouth. We have had to have many teeth removed to make room for new ones. He is also prone to decay, no matter how well he brushes his teeth.” 12 years

Genitals

A large recent review found that most boys regardless of age will have enlarged testes but researchers found no evidence of increased hormone levels linked to this, and are unsure what this finding means. The same review found no increase in minor genital anomalies such as undescended testicles or hypospadias, where the hole usually at the end of the penis is on the underside instead (Ross 2009; Bardsley 2013). A review of Unique members aged 5 – 18 suggested that enlarged testes may be less common than the research suggests: just 3/21 families confirmed this feature, although the increase in size would not be something most families are aware of.

Medical issues

■ Asthma

Most boys with XYY do not have asthma, but it is more common than in the general population. Asthma was found in almost 39% (35/89) of boys in one large recent study, compared to a general population level of 9.6% (Bardsley 2013). The authors point out that the extra Y chromosome may be amplifying the risk of atopy, as there is a greater prevalence of atopy/asthma and a reduced relative airway size in boys compared with girls. The Unique 2014 survey showed asthma at a lower frequency in 5/20 boys, of varying severity, but all boys were using inhalers, and one had been repeatedly hospitalised with asthma. Unique also found a high rate of chest infections in the first three years of life or later in childhood, with 14/21 families reporting this.

■ Seizures

There is a possibility that seizures are more common in boys with XYY than in the general population. The most comprehensive study to look at this found that among boys diagnosed prenatally, 1/35 had seizures, giving a rate of 3% compared with 1% of unaffected boys. They are treated with standard anti-epilepsy drugs.

The Unique 2003 survey also suggested that among this highly selected group, seizures were more common than expected in the general population. Eight out of 32 family reports (25 per cent) mentioned seizures; this was by far the most common medical condition mentioned, and can be explained at least in part by the fact that boys with epilepsy are more likely to have their chromosomes examined. Two boys outgrew them in adolescence and there were no reports of seizures occurring in adults.

In the 2014 survey, 2/21 boys had seizures, in one case fever-related. Both boys were diagnosed postnatally.

■ Do men with XYY die younger?

Two large follow up studies of men with XYY have revealed that they are likely to die younger than other men. One study of all men diagnosed with XYY in a single country, Denmark, showed that life expectancy for men with XYY was 10 years

less than for others, with men with XYY dying on average at 68 years rather than 78. Both studies showed an increase in deaths from respiratory diseases, and the Danish study also showed more deaths from cancer, neurological diseases and accidents. The underlying reasons for this are still not understood, but one possibility is men's socio-economic conditions [Swerdlow 2001; Stochholm 2010; Stochholm 2012].

■ Fine motor control. Low muscle tone

A number of studies have looked at motor control and coordination in boys with XYY. Long term screening studies found that in general boys had reduced fine motor coordination, meaning that boys were more likely to face problems with tasks such as writing, drawing and cutting with scissors, as well as balance. In two later studies on prenatally diagnosed groups parents reported motor delay or lack of coordination in 25-35% (3/12 and 4/15) of boys. Later studies assessed this independently and found that the XYY boys performed slightly less well on tests of strength, speed and dexterity [Ratcliffe 1999; Ross 2009; Leggett 2010].

Mild tremors were common and could be seen while resting or during movement (intention tremor) in 43% (39/90) boys in the largest cohort study. In most boys the tremor is too mild to affect writing. Low muscle strength and tone was also noted in half of the 35 boys prenatally diagnosed with XYY in this study. While these symptoms are usually mild they might impair handwriting or other skills and if this is the case extra support in school or occupational therapy might be needed. Other studies confirm these findings, showing intention tremor as both more frequent and more intense in XYY [Theilgaard 1986; Ratcliffe 1999; Geerts 2003; Bardsley et al. 2013].

These observations are amply supported by a Unique survey from 2003, in which 36 families (84 per cent) recorded a problem with either fine motor control or balance [Unique]. Unique's survey in 2014 again confirmed these findings, with boys diagnosed during childhood more likely to be affected. The low muscle tone had multiple effects, on balance, posture, stamina, sports activities, as well as on writing. Tremor was less common than in the studies, with only 2/21 boys having a hand tremor.

Educational features

Speech and Language

Speech and language is a common area for concern, and having an extra Y chromosome increases the likelihood that a boy will have speech and language difficulties. Small early studies suggest speech delay in up to half of all boys with XYY, making it more than twice as common as in boys without an extra Y chromosome [Ratcliffe 1999; Geerts 2003]. Larger, more recent studies show that some speech problems were found at all ages - although not in all boys - and that at school boys tended to struggle with language and verbal tests, even though IQ (intelligence quotient) was typically in the normal range. In particular they struggled with figurative or ambiguous language, expressing themselves

and verbal memory. A small proportion developed slight verbal tics such as clicking or stammering (Ross 2009; Leggett 2010; Bishop 2011; Cordeiro 2012; Tartaglia 2012).

Additionally, the UK study of 58 boys, some of them members of Unique, that drew attention to the high rates of autism spectrum disorders - 10-20 times higher than the estimated prevalence in the general population - also found that among boys who did not have autism, communication profiles suggesting mild autistic features were common (Bishop 2011). Parents reported to the researchers a relatively good understanding of tone of voice, gesture and body language in these boys, but communication was often a difficulty. The researchers said that while boys found it challenging to express themselves clearly, they had a range of interests and could rephrase sentences others might not understand. The boys diagnosed in childhood tended to find all aspects of communication challenging, especially understanding the meanings of words and how they might change with context (DIESC study).

A small study of boys diagnosed during pregnancy found that the age at which boys spoke their first words was 12-42 months (Lalatta 2012).

Evidence from Unique shows that speech delay is, as expected, much more common among boys diagnosed after birth than among those diagnosed before. In both groups, though, there are boys with speech delay and difficulties, and boys without. There is a wide range of severity across both groups, with boys diagnosed after birth generally - but not always - having greater difficulties. The great majority of boys receive speech and language therapy and outgrow most of their speech difficulties, so that this is no longer a problem among many adults.

The most common speech difficulties found at Unique are speech delay, especially in talking, putting words together, talking clearly so that others can understand, and using more complex words. Understanding is generally ahead of talking, and ranges in the Unique experience from advanced for age to somewhat delayed, although less than talking. Weakness or floppiness of the facial muscles (oral hypotonia) may underlie the unclear speech, and responds well to speech therapy. A difficulty in summoning words or the correct word is common, leading to slow delivery and difficulties in conversation. Sentences may be short, with a simple 'telegraphic' structure. Speech problems are especially noticeable in social situations. At the more severe end of the spectrum, boys may receive a diagnosis of a specific disorder such as speech apraxia (where someone is unable to say what he wants to). As noted in the medical literature, a small minority of boys develop a stammer or a verbal tic such as clearing the throat or making a repeated 'aah' or sucking sound, or repeating a word or sound involuntarily, and a stutter can persist into adulthood. Among boys under school age, speech delay could be severe, with vocabulary limited to less than 5 words, and individual boys showing a speech and language delay of 2 years. Speech clarity was a general concern.

Among boys of primary school age, there was a general improvement, but boys

of 9 or 10 years still had difficulties with conversation, complex words, and continuous narrative. Speech clarity improved generally but remained a problem for a few, especially when talking at speed.

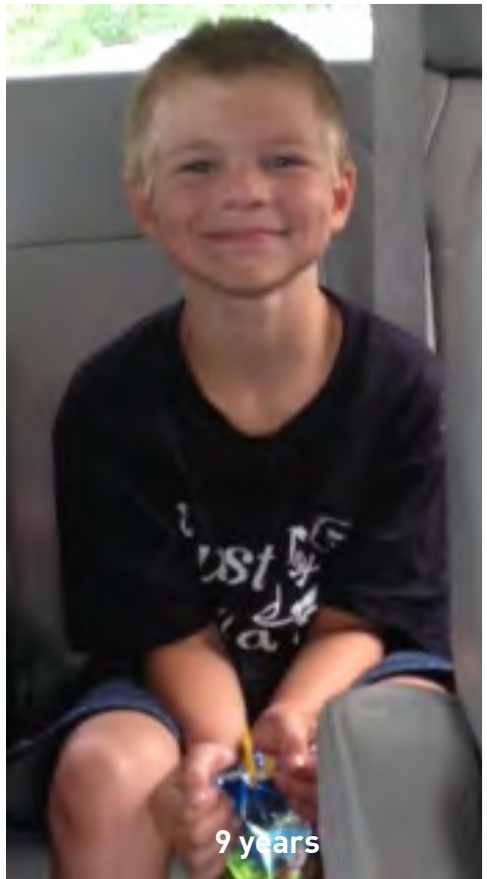
Among adolescents, there was a wide range of speech and language ability, with some boys speaking fluently, others having problems finding words, building long sentences, speaking coherently, using language in social situations, and sometimes with understanding or with processing speed. Problems with speech clarity appeared to be less than in younger boys.

It is extremely common – although not universal – for boys to understand plain language only, and not to understand sayings, idioms, slang, jokes or irony. They may need the funny side explaining to them. Examples include: *If someone says it is raining cats and dogs, I look outside (teenager with XYY); When my husband hurt himself, he was kidding around and said 'See what you did'. Well my son with XYY got so upset he broke down and cried; If someone says 'Wait a minute', when a minute is up, he tells us it's time to get going.*

Most adults with XYY told Unique that they no longer had any speech problems, outgrowing their speech delay (generally with speech and language therapy) in childhood or adolescence. A small number of men carried speech difficulties over into adulthood, including unclear speech, some 'slight slurriness', being stilted in conversation, or not starting conversations, and difficulties finding the right word or tense.

Being unable to communicate is frustrating. Some handle the problem calmly, taking people to what they want, or showing them physically; others retreat and are quiet other than 1:1 or go into meltdown (tears); but growls of exasperation and temper outbursts are common, especially in young children. The evidence from Unique is that anger outbursts lessen as boys get better at saying what they want and develop other skills, so they usually improve in adolescence and have gone by adulthood.

“Slower and a bit less natural sounding, monotone sometimes. But he keeps up with jokes, idioms, slang etc.” 12 years



Learning and schooling

A survey of all studies to date of boys diagnosed before birth showed a slightly lower overall IQ (intelligence quotient) than you would expect for the family, but very close to the population average of 100. Verbal IQ was also lower than you would expect, but again was generally within normal limits for the population at large (Leggett 2010). In a more recent study, cognitive deficits were generally mild, most children attended mainstream schools and some performed in the normal or superior range (Bishop 2011). The largest more recent study confirmed these findings: among 36 boys diagnosed before birth, average IQ was 102, while among 44 boys diagnosed later for a variety of reasons average IQ was 85. Verbal IQ was 101 in the prenatal group and 82 in the postnatal group (Bardsley 2013).

The studies show that having an extra Y chromosome makes it more likely that a boy will need some learning support at school, and importantly that any learning difficulty in XYY is as responsive to help as learning difficulty in the general population (Götz 1999; Ratcliffe 1999). An early study (Ratcliffe 1999) found that half of a group of 19 boys diagnosed at birth needed help with reading. The most recent survey in the UK found that boys with XYY were almost five times as likely to need special schooling as the population average. Even boys diagnosed before birth were much more likely to need a formal support statement or programme than boys with XY chromosomes, and this need was extremely common among the boys diagnosed after birth. Despite this, most of these boys coped well with classroom support in mainstream schooling. Around a third attended a special unit or school, usually being referred at ages 11-13 because of lack of resources for learning support in large high schools. Boys in this survey were reported to be good at mathematics, although many found English a little more challenging.



Parents reported that getting help at school made a big difference to their son's happiness, and they noticed an improvement in progress when help was in place (Bishop 2011).

Findings among Unique members confirm this.

There is a range of educational difficulties, from boys who are keen, successful learners and leaders to boys who struggle socially, academically and behaviourally at school. The boys who find it easy to learn are more likely to have been diagnosed before birth, but some boys diagnosed after birth also have no learning difficulties. Among boys with no formal diagnosis of a learning difficulty, difficulties still occur, mostly with reading, words (dyslexia is common) and the physical act of writing, or with processing information. A more general learning difficulty, affecting all areas of the curriculum, is not common and in Unique is found very much more often in boys diagnosed during childhood; indeed, the learning delay may be one reason for the chromosome test.

What sort of school?

The great majority of boys start their education in mainstream (regular) schools, and most stay in this sector throughout their education, with some selected for schools for brighter children. Boys diagnosed before birth are more likely to stay in mainstream schooling, but among Unique members half of the boys diagnosed after birth were still in a mainstream secondary school after the age of 11. The switch into special education often came in the early years of secondary schooling, and support was provided for behavioural as well as learning difficulties. A minority of boys did well in home schooling. At the far end of the spectrum were a very few boys who attended special residential schools.

As found in the studies, many parents found that getting educational support was a big help, and some reported a sharp drop-off in attainment when the support was withdrawn. The amount of support varied a lot, from boys who just needed reminders to stay on task, parental help with homework or extra English, reading or writing, to boys who needed special schooling.

Parents said that the best learning environment was calm, without distractions and with low background noise, structured, and in a small group or 1:1. Sessions were best kept short with frequent movement breaks. Learning was better if it was oral, practical or visual, minimising handwriting. Computer-based learning worked well for some. Outdoor learning could be helpful. Boys needed frequent encouragement, and the pace needed to be appropriate.

Strengths and weaknesses

Learning strengths often mentioned by parents included mathematics, science, art, visual learning, practical subjects (woodwork, cookery) and, when interested, curiosity and memory. Slightly less common strengths include physical activities (but not necessarily team or contact sports), and spatial awareness. Weaknesses include, most often, literacy, including both reading and writing, motivation (very hard to persuade to do something), coping with pressure, and above all, concentration and staying on task.

Almost every boy had some difficulties with focus and attention, and needed support to keep up his concentration. Learning tasks were best when short, with frequent breaks. Specific writing difficulties were also common. Many boys had

problems holding a writing implement due to low muscle tone in the hands and in a few cases, a hand tremor. Writing was often described as sloppy or untidy. Writing for some improved over time, but more severely affected boys used a keyboard or scribe. However one boy has 'beautiful cursive'.

With their additional height, one might expect sport to be a strength, and for some boys it is. The low muscle tone that has been reported as a feature of XYY (Bardsley 2013) does not prevent enthusiastic and often skilful sports activity. Families mention a very wide variety of sports and activities, with boys enjoying and excelling at sports as varied as cycling, swimming, fishing, water polo, rugby, sailing, horse riding and bowling.

Behaviour at school is an area of concern to many families – although a few report exemplary or excellent behaviour. Most families report that their son has been picked on or bullied – because of his height, his immaturity, and his difficulties getting on with other boys. Many say that their son is disruptive at school, and this is especially common among those diagnosed after birth. Some boys have been excluded.

As most of the studies have focused on younger children, there is not a lot of information on what boys do after leaving school. One study, published in 1999, found that 5/19 boys had gone on to university or technical college (Ratcliffe 1999). Within Unique, the 2014 survey showed that among 9 boys diagnosed prenatally, only one left full time education before 18. Their highest level of qualification was vocational for two; GCSE – an academic test typically taken at 16 – for 2; A levels – an academic test typically taken at 18 – for 1; and university degrees for 2. Specialist subjects included computers, music production, photography, art and animation, sports coaching and education science. Five had vocational training in subjects including performing arts, media, drama, engineering, art, music, sailing and uniformed services training. Adults still in full time education had done a variety of jobs including cleaning windows, working in a cafe, cleaning, assembling kits and gardening. Jobs included working in a warehouse; assistant shop manager; refuse collecting; and driving. Among boys diagnosed in childhood, there is a broad range of outcomes from those leaving school with a full set of examination results to others with no qualifications, or who do not attend school after the age of 14 or 15. Their skills reflect their academic attendance: at one extreme are young men who are only just able to read and write; at the other are men with a curriculum vitae rich in vocational experiences: fire fighting, cardiopulmonary resuscitation, phlebotomy, painting, decorating, legal work, motor mechanics, welding, administration and warehouse work. Most young men have been employed, in occupations as varied as nursing, catering, dog walking and working as a cashier.

“He had a quiet corner made available to him when he felt unable to cope when he was younger. At the age of 9 he received 10 hours of one-to-one support a week to help him manage his outbursts of anger. He is now succeeding at a

small school where he is well known.”
10 years

“Usually task-orientated unless he knows something fun is planned for later. Actually excels in writing. He has beautiful cursive.” 12 years

“C has speech and language delay, a short concentration span and easy distractibility, lack of confidence and social skills. He is receiving 12 hours a week of support at school, and has a lot of parental backing. He does not have angry outbursts. This year in a mainstream school he achieved 10 excellent end-of-term grades, sixteen good grades and one satisfactory grade.” 13 years

“He is a very boisterous, energetic boy who can be affectionate but continues to suffer rapid mood swings. Be persistent. They wanted to put my son in schools for behavioural problems which I did not feel was the correct thing to do as he copies things and is easily led.” 16 years

“C is in a preparation for work group, and is out of the house for part of the day most days on courses and doing voluntary work. It would be good if he could be fully employed either voluntarily or paid.” 24 years



Social interactions and Autistic Spectrum Disorder

“He also has the diagnosis of autism for which there is more help available. We use autism as his diagnosis because the services recognise this and strive to find options for these young people.” 22 years

Recently a number of studies have shown a link between XYY syndrome and autism spectrum disorder (ASD). One possible reason for this is changes in diagnostic practice, so a disorder previously considered to be a language or communication disorder might now be considered a disorder within the autism spectrum.

All studies found a wide range of results and at least two thirds of boys did not have a diagnosis of ASD. However, the risk of developing autistic behaviour was significantly raised both in boys diagnosed before birth and boys diagnosed later. Autistic behaviour was found less often in boys diagnosed before birth, and characteristics were more severe in boys diagnosed in childhood.

Rates of diagnosis are controversial, because they depend on whether boys diagnosed after birth (and therefore boys with problems) are included or not. In two different studies, looking only at boys diagnosed before birth, rates ranged

from 11-20% (1 in 5-10) (Bishop 2011; Bardsley 2013). In another study, 19% of 26 males diagnosed postnatally had ASD (Geerts 2003).

In the boys who were not diagnosed with ASD, mildly autistic behaviours were common, although this was very variable. It was noted in several studies that the likelihood of a diagnosis of ASD did not appear to be linked to intelligence or the diagnosis of speech and language difficulties. It was also stressed that not all children with an extra Y will have social difficulties but if they do it may be useful for the clinician to know about it. One of the studies points out that all the boys had a normal social motivation score, which is positive in terms of interventions as it means that they want to interact with others but may misinterpret cues. However they suggest that care should be taken by clinicians not to dismiss a diagnosis of ASD due to this (Bishop 2011; Cordeiro 2012; Ross 2011; Bardsley 2013).

Among Unique families surveyed in 2014, a formal diagnosis of autism or an autistic spectrum disorder was present in almost half. Rates of autistic behaviours were very much higher among those diagnosed after birth, so those with some kind of developmental problem, autistic features were evident in two-thirds. One child was diagnosed with autism at 4 but lost the diagnosis as he matured.

For many families, a diagnosis of autism is helpful because it opens the way to better services, but one family commented that despite the diagnosis their 12

year old son does not respond to strategies aimed at other children with ASD because he is so sociable, and is not routine-bound.

“The autism diagnosis didn't 'fit'.”

Does early intervention help boys with XYY?

Given boys' vulnerability to communication and behaviour disorders, does it help to carry out regular checks in childhood on boys diagnosed either before birth, or coincidentally? With specific attention to speech and language, could aggression due to frustration and low self esteem be reduced?

The evidence from Unique is that learning support and speech and language therapy are extremely helpful, and various researchers suggest regular six-monthly examinations for the first 3 years, as well as a specific focus on learning difficulties, attention deficit/hyperactivity disorder, and autism spectrum disorders (Ross 2009; Lalatta 2012).



Behaviour issues

Attention and concentration. Activity and hyperactivity

It is generally agreed that boys with XYY are vulnerable to easy distractibility and hyperactivity. Multiple studies of both boys diagnosed before birth and after have shown raised rates of attention deficit hyperactivity disorder (ADHD), and these are supported by parental reports. However, when does energetic become overactive? And when does overactive become hyperactive? In the group of 57 boys tested in the UK and eventually reported in the medical literature by Bishop 2011, hyperactivity and inattention were indeed common, found in around one third of boys regardless of when they were diagnosed. When considered in more detail prenatally diagnosed boys tend to be described as restless, hyperactive or inattentive, and were often described as busy and energetic. Overall they were described as energetic boys who may have difficulty concentrating but were great fun! (Diesc 2010)

The increased distractibility and attention problems were found in most of the early studies with rates among boys diagnosed before birth ranging from 10-60% of boys. In one study, half the boys needed support for attention problems and in most this became evident around the age of 2½ or 3. The boys' primary school teachers frequently reported restlessness, meandering or running about when the boys were expected to sit or stand quietly (Walzer 1990). Further studies showed that 11% to 21% of two small groups of boys diagnosed prenatally were given a diagnosis of ADHD (attention deficit hyperactivity disorder) (Linden 2002; Geerts 2003). One review found that there were few reports of ADHD diagnoses; however, multiple study sites reported descriptions of problems with attention, distractibility, impulsivity, and behavioural regulation (Tartaglia 2012).

Since then three larger studies have looked at behaviour and ADHD, all including a biased mix of boys diagnosed prenatally as well as later. There is a lot of variation between studies and the numbers of affected boys are significantly higher in more recent studies, but all agree that boys with XYY are at an increased risk and suggest they could be screened for ADHD (Bishop 2011; Ross 2011; Tartaglia 2012; Bardsley 2013).

There is very little reported information on how to help boys with ADHD in XYY, but one study of 2 boys found that methylphenidate was helpful (Ruud 2005), and a larger more recent study found that overall three quarters of boys were helped by a stimulant medication such as methylphenidate (eg Concerta, Equasym, Medikinet, Ritalin) or an amphetamine (Adderall, Elvanse). With increased irritability a frequent reason for stopping taking the medication, the authors suggest low starting doses with gradual increases. A much smaller number of boys were being treated with non-stimulant drugs including atomoxetine (Strattera), guanfacine (Intuniv, Tenex) or clonidine (Catapres). The authors suggest that before assigning an ADHD diagnosis or starting on medication a full psychological assessment is carried out to help determine whether other

learning disabilities, speech/language disorders, or emotional symptoms are present, which may need to be included as part of a comprehensive treatment plan (Tartaglia 2012).

Many families in the Unique 2003 and 2014 surveys mentioned poor concentration as a cause of their son's education difficulties. In the 2014 survey, 5/6 boys diagnosed prenatally and 14/15 of those diagnosed postnatally were considered by their parents to have concentration problems. The concentration problems were as common in the teenagers as in the younger children – though this could be because school expectations of older children are greater. The youngest child to receive a diagnosis of ADHD was 3, although the mother of a young man of 34 commented that she was aware of her son's hyperactivity by twelve months but could not persuade doctors to agree with her.

Parents found it helpful to discuss their son's concentration problems with the school. Some schools offered shorter learning sessions, more breaks and physical activity in the breaks. Some boys needed learning support to keep them on task. A small number of boys were on prescribed medication, specifically methylphenidate.

Sixteen boys (33 per cent) in Unique's 2003 survey were described as hyperactive or had received a diagnosis of attention deficit disorder. In the 2014 survey, 3/6 boys diagnosed before birth were described as overactive, but only one was hyperactive and one diagnosed with attention deficit hyperactivity disorder (ADHD). Among those diagnosed in childhood, 11/15 were described as restless and overactive; 6 as hyperactive; and 7 had a diagnosis of ADHD.

Parents' strategies focus on regular and demanding physical activity, including daily sport. Some boys, and some adults, are medicated with methylphenidate.

"We run him in a park/ on the beach for a couple of hours." 6 years

"Sport every night." 14 years

"We get him to go for walks or carry something heavy." 15 years

Behaviour : other issues?

Do boys with XYY have behaviour difficulties other than concentration, activity levels and behaviour that might fall within the autistic spectrum? The answer seems to be that while many boys will have no behaviour problems, overall there is an increased risk, particularly among boys diagnosed during childhood.

Tantrums? Impulsive? Aggressive?

Temper tantrums, impulsiveness and aggressive behaviour were found in the early studies, and have been confirmed in larger, more recent studies in situations where boys were frustrated. This does not by any means mean that every boy is affected, but it does mean that boys with XYY whether diagnosed before or after birth are vulnerable to this sort of behaviour (Ratcliffe 1999; Linden 2002; Ross 2011; Lalatta 2012; Bardsley 2013).

The UK study of 57 boys with XYY found much higher rates of 'concerning

behaviour' in boys with XYY than in their brothers, and these behaviours included temper tantrums. Parents reported that temper tantrums were usually caused by frustration, often as a result of a build up of relatively minor incidents. Some parents reported being able to prevent outbursts by calming the situation before frustration builds up (Diesc 2010).

The Unique surveys showed that anger, aggression and to a lesser extent swearing and verbal aggression were common in boys of all ages whether diagnosed before or after birth. The 2003 survey showed that temper tantrums almost certainly occur independently of frustration at not being able to communicate easily, although they may be triggered by it. Bouts of aggression occur in otherwise happy, loving boys. They can start as early as 15 months, but more typically develop around age 5 to 6 and in some do not occur until the teen years. Triggers for tantrums include children being denied or stopped from doing what they want and social stress, including stress at school, tiredness and unexpected changes in routine. Behaviour during a toddler tantrum can include throwing objects including furniture, hitting people (including strangers in the street), headbutting, biting and spitting. As boys get older, the angry outbursts and tantrums may lessen, but do not always do so. They may become more publicly aggressive or violent, and behaviour includes swearing, shouting, screaming, kicking and pinching as well as offensive rudeness and extremely forceful demands and threats.

Many parents need professional support (such as a behaviour nurse) to cope with their son's behaviour. Helpful techniques include time out; breathing calmly; talking it through; having a place to let off steam; a weighted blanket; planning ahead to avoid trigger situations; breaks in activities. Quite a few families have needed professional support and some boys have had medication (typically risperidone) to calm them.

Sociable? Immature? Easily led?

Again, studies have repeatedly found that while some boys are unaffected, difficulties in social relationships are common (Ross 2011; Lalatta 2012; Bardsley 2013).

The UK study of 57 boys with XYY found that many families expressed concern at social skills and the Diesc report to parents makes interesting reading. They did find higher rates of 'concerning behaviour', including difficulties reading others' emotions and being easily led, and 'some of the boys were observed to find interpersonal relationships challenging, at times finding it difficult to relate to others and understand their point of view. Despite this, families found that the boys were relatively good at saying sorry, and were usually polite. Yet over a range of different situations, only 1:5 prenatally diagnosed males showed difficulties in social situations. This was assessed over how well they played with others, shared, and coped with the disappointment of losing, their understanding of their own emotions, and recognising emotions in others,

leading on to their understanding that others have different interests and thoughts, and finally how well they behaved when introduced to others, their manners, and changes of routine. In particular many families commented that their son found it challenging to relate to peers, despite being keen to make friends and be part of a group. Some families were concerned that this had led to their son behaving badly at school to try and fit in with or impress other boys. When these aspects are considered in more detail it becomes apparent that these boys are relatively good at understanding play, sharing, and coping with losing, but find it more challenging to understand others' thoughts, feelings and emotions. This pattern is also apparent with regard to postnatally diagnosed boys who find social skills particularly challenging, however, like prenatally diagnosed boys, they are keen to try to make friends (Diesc 2010).

Findings from Unique confirm parental concern. In the 2003 survey, 58 per cent of Unique families noted a lack of social skills, while the 2014 survey showed that most boys wished to be sociable but did not always know how. In particular families said their sons were generally **not** empathetic. The parents of three adult men with XYY commented that their sons found group situations especially hard to handle and were therefore disadvantaged at school. Once they left school, their difficulties faded. In the 2014 survey families frequently commented that their son found it easier to be sociable with people younger or older than themselves.

The great majority of families also commented that their son was easily led and could be gullible. To cope with this, parents controlled the company their son kept as best they could, and talked over possible alternatives to doing what others suggested.

Emotional immaturity and impulsiveness, exacerbated by the disparity between apparent and actual age, was noted by half of the Unique families in the 2003 survey.

Other behaviour

On other aspects, such as anxiety and depression, study outcomes are conflicting, with some showing increases at least in parental perceptions, although not in boys' view of themselves (Ross 2011; Bardsley 2013). The evidence from the prospective studies is that a minority of boys have a heightened negative response to stress, with rates of anxiety and depression above those for the general population (Ratcliffe 1990; Linden 2002).

In the Unique 2014 survey of 12 adolescents more than half reported high anxiety levels or a diagnosis of anxiety. Families said their son found life stressful, or got easily upset when faced with challenges. There was a wide range of severity, but at the more severe end adolescents have become suicidal when faced with a challenge they could not cope with.

Some behaviours diminished with age and consistent management, including impulse control, getting easily upset and feeling hurt, and obsessive or

compulsive behaviour.

Families tried to cope using these strategies: making expectations clear and consistent; using social stories; talking over the problem and looking for solutions; and discussing changes before they occur.

“He is afraid of thunderstorms etc, and roller coasters too. He takes escitalopram (Lexapro, Cipralext) for this.” 12 years

“He has a visual timetable for routines and school, and joining the army cadets has been great.” 14 years

A small minority of Unique families observed problems with authority in their son, particularly in adolescence and when he disliked or did not respect the person in charge. Some young men assumed the role of leader themselves. Others fell foul of the law.

But Unique has no evidence that this behaviour is more common in boys with XYY than in other boys.



Coping with behaviour in boys with XYY

Unique families report greatest success when they can be patient, calm and firm in their approach. Positive parenting techniques help, with predictable routines and clear boundaries and expectations. Talking problems through and encouraging the boy to talk is helpful, especially when problems are due to emotional immaturity. The home atmosphere needs to be ‘firm but flexible’ and boundaries need to be clearly set. Boys up to age 11 may respond to rewards and star charts and by secondary school age boys may be motivated to help themselves. But many parents admit that despite their best intentions, the best support and the most structured home environments, the answer was professional help and medication. One parent described medication (accepted reluctantly) as ‘an oasis’. Counselling and prescribed medication as well as natural maturity improved behaviour in one of the studies (Ratcliffe 1990).

Interventions

Many Unique families have been offered psychological or psychiatric help or help with social skills. In some cases parents saw psychiatrists separately to learn how to manage their son’s behaviour, but with increasing age and certainly

from puberty, behavioural intervention or psychiatric help was offered direct to the boy.

No single programme answers all the needs of a family affected by XYY. Three themes emerge from the 2003 Unique survey:

- Families need consistent, imaginative and proactive help. They value interventions that develop skills within a framework shared by other children without a chromosome disorder
- Boys develop best in less stressed families. Having a boy with XYY behavioural problems is intrinsically stressful and support services need to direct Interventions to the family as well as to the boy with XYY
- Support needs to continue beyond adolescence into adult life.

Parents' insights

Can be a charming, lovable little boy. On a bad day he is hard work: tantruming, no concentration on anything, obsessive with doors. 3 years

Quiet, placid, very affectionate. Doesn't understand emotions like sadness or anger which makes disciplining rather hard. Temper tantrums and hitting out/throwing increasing. Wandering off and getting lost and unresponsive to his name being called increasing. In spite of all this, an absolute joy. 3 years

He can be the kindest, most gentle, sweet boy but can turn if told off and gets frustrated regularly. He hits out, throws things, kicks, bites, hits ..., but will calm when given time out. 4 years

Well behaved. However, easily upset if he perceives he has done something wrong or if he has been told off. 7 years

He is very sweet, very friendly, and very polite. He loves to help. He doesn't have a lot of friends because he just doesn't seem to know how to interact with them. He is easily frustrated when he doesn't know how to do something and we cannot seem to get him to understand that the way to get better at something is to listen and learn. 9 years

Excellent on 1:1. Can get overwhelmed and anxious easily. 11 years

Doesn't focus on tasks well and can easily spend hours playing computer games. Can get occasionally upset if losing a game, or cannot come up with an answer to a question. 11 years

Always been active, limited concentration, has calmed down a lot of late. 14 years

Wakes early and takes Ritalin. Disorganized and chaotic until this kicks in and then really great. At school and then home – Ritalin again in afternoon. Now spending most of the time in his room playing computer games despite trying to get him to do work. Tries to play with his brother and sister but this is causing lots of stress as it ends in fights. Very uncooperative with general family tasks and argues over everything. Extremely remorseful and loving after outbursts. 14 years

Attention seeking, answering back, tends to be very hyper at end of day, unchanged essentially from age 4. 15 years

Well-mannered, polite and happy child who seeks friendships. Loves animals and the outdoors (we live on a farm). Plays nicely with his younger sister most of the time. Extreme inability to regulate emotionally. He seems to have a constant fear of safety to himself and sees an injustice to himself if accidentally touched, someone interrupts play or the rules are changed. He never said he did not want to go to school and would always put himself back into situations that had proven difficult previously. He seemed unaware overall of how he had damaged friendships and trust of others and he shows little empathy, remorse or understanding of the complexity of situations. 15 years

No internal control so needs external ones. 17 years

Now typical teenager, sometimes good company and sometimes grumpy and uncommunicative. 18 years

It was as if we were dealing with a teenager for 15 years. 34 years

He's often a real gentleman but can be nasty if provoked. Bullying reduced his confidence to nil.

Parents: what can help

Be there for him until he realises that he is the only one who can help himself. 14 years

Keep a simple set of rules and do not allow straying from them without an immediate consequence. But give praise at every conceivable moment. Avoid pressure, don't ask too much or too little and take one step at a time. 19 years

Seek help as early as possible. 22 years

Never give up. 26 years

Behaviour difficulties **Sexual behaviour**

Unique receives occasional queries about sexual behaviour, particularly in adolescents with XYY. We have no information to suggest that sexual behaviour is any different to adolescents with XY.



Early reports of criminal convictions

The great majority of men with XYY lead law abiding lives, do not behave antisocially and do not have criminal convictions. Early reports of men in penal institutions led to a belief that raised testosterone levels in men with XYY leads to aggressive behaviour. This research should be viewed with extreme caution, because it relies on small, selected groups, and other studies found normal testosterone levels in boys and men with XYY. Follow-up studies of men with XYY have indeed found an increase in some criminal convictions, but they were not related specifically to aggression, and more recent research has shown firstly that the increased conviction rate was associated with lower intelligence, and also that it might be explained by poorer socio-economic conditions (Rudd 1968; Witkin 1976; Schiavi 1984; Ratcliffe 1999; Stochholm 2012; Bardsley 2013).

Puberty

Repeated studies have shown that puberty is generally little different in boys with XYY to boys with XY. One of the early studies found that it started on average six months later than in XY boys but then proceeded normally. Pubic hair grew on average more than a year later in boys with XYY, around the end of the fourteenth year. In a larger and more recent study, puberty in some boys occurred early in the age range of childhood (Ratcliffe 1990; Stewart 1990; Linden 2002; Bardsley 2013).

As adults

There is not enough information about how adults with XYY get on in life. One of the reasons for this is that with the great majority undiagnosed, there is no reason to believe that they do not lead normal adult lives. The handful of studies on adult outcomes indicates that most individuals with an extra sex chromosome are able to live independently and form normal adult relationships (Leggett 2010). Recently, a study of all men in Denmark known to have XYY has shown a drop in socio-economic status (Stochholm 2012).

“I feel I have had the best upbringing by my mum. She is a single mum and has been very understanding but has never used my condition for excusing bad behaviour or poor judgments from me. She has pushed me and the education system all my school life. I did well at school – better than the teachers thought I would do. My mum believed in me 100%. I still need stuff explained to me many times if it’s new to me, but I get it in the end. I am about to start level 2 welding and fabrication training. I really enjoy it. My future goal is to be a deep sea welder. Big money!” 18 years

“He leads a normal fulfilling life and enjoys and works hard to make his own life. He sometimes still struggles around peer groups but has friends and has had girl friends. He sometimes misses the nuances of social niceties and is always too keen to be overgenerous in the hope of people liking him, but with maturity he has started to learn boundaries and self restraint.” 19 years

“Currently I am employed as a first responder firefighter. Every day I am continuing to further study and improve my emergency services/ fire career. I am also attempting to help give back to the community I serve by helping teaching high school students about careers in EMS fire. I am also an active member of the Lions Club. To the parents out there I just want to let you know that throughout all of the difficulties that you may encounter in your child’s life, things will get better. They may even become a firefighter/ medic like myself. Starting next year I will work on starting to study to become a paramedic.” 27 years

Work

Among the men diagnosed before or at birth, follow up of men in Scotland showed that most boys go on to play a useful part in their community and to hold down jobs as varied as a self employed businessman, a chef and a community service worker. Out of 19 boys, two studied engineering at university and three went to a technical college (Ratcliffe 1999). Early follow up of men in Denmark showed that one was majoring in science at college, while three others planned careers as a mechanic, engineer and farmer (Nielsen 1990). Longer and more detailed follow up of men in Denmark, including those diagnosed before, at and after birth, shows that income was lower, and men were also more likely to to cease working earlier in their lives (Stochholm 2012).

The Unique 2014 survey showed that out of 9 men diagnosed before birth and now aged from 19 to 38 years, three were still students, one had worked as a sailing instructor, one was working in a warehouse, one in gardening and photography, one in a shop as assistant manager, one in a variety of jobs including sales, car cleaning, refuse collection and driving, one was in supported employment, and one was not working.

Among the 15 men diagnosed as children because of behaviour, speech, learning or development concerns, one was working as a catering assistant, one had worked in a factory but was currently not working, one had been a voluntary dog walker, one was a firefighter with ambitions to further his career, one had done a range of voluntary work and was in a government-sponsored preparing for work scheme, one was on an apprenticeship scheme and the rest were not working, or were still in education.

Living arrangements

Follow up of all men in Denmark diagnosed with XYY since 1960 shows that they were generally five years older than other men, on average 30 years, before they were living with a partner (Stochholm 2012). The Unique 2014 survey showed that of the 9 men diagnosed before birth, 5 were living at home with their parents as adults, two were living independently, one with his girl friend, and one was in supported living. Among the 14 men diagnosed after birth, 4 were living independently either alone or with their partner or own

family, seven were with their parents and one was in a secure unit. Three men in all had a long term partner, and one, diagnosed in childhood, had children of his own.

Freetime activities

The 2014 Unique survey showed that taking the 24 adults together, 9 listed computer games as a freetime activity, and 9 listed physical activities including dog walking, weightlifting at the gym, rugby, football, sailing, cycling and walking. Four took part in sports, one playing rugby and sailing at county level, and another playing disability football. One plays the tuba in a band.

Health

Of the health issues listed by the 23 adults in the Unique 2014 survey, at least four – hand tremors and low muscle tone with stiff joints, asthma and epilepsy – are likely to be associated with the XYY condition. Overweight may also be associated, as the most recent large survey showed that almost twice as many boys had a higher waist measurement than in the general population (Bardsley 2013). Other health concerns unlikely to be associated with the extra Y chromosome were psoriasis, varicose veins, and food allergies.

Mental health and behaviour in adults

An important question for parents is whether their son will outgrow any behaviour difficulties. The evidence from Unique is that behaviour in most boys does indeed improve, and while some adults are aware that they have a quick temper, it is under control. There is a small number of young men whose behaviour continues to be hard for them to handle and may give cause for concern, and who need professional support and intervention. Early studies also showed that more men with XYY than in the general population were referred for psychiatric evaluation (Ratcliffe 1999). When these men were examined in detail, it was found that while they did show more antisocial behaviour as adults than their peers, in most cases this fell short of clinical concern (Götz 1999). More recently, a large study of men in Denmark also found an increased risk of social maladjustment (Stochholm 2012).

This general picture is supported by information from the Unique 2014 survey. Of the 9 men diagnosed before birth, 3 gave no behaviour or mental health concerns. Three men said they had 'a bit of a temper', although this was only linked with aggression in a young man with learning difficulties; one was easily upset; one had mood swings and social difficulties; and one had a possible stress induced psychosis with agoraphobia, anxiety and panic attacks. One man noted that he 'overtalks' people, and finds it hard to make friends.

Of the 14 men diagnosed in childhood, 3 had no behaviour or mental health concerns. Three men have an anxiety disorder, and one has obsessive compulsive disorder. One reacts strongly to stress, and can be violent. Three have socialising difficulties; two are easily upset, and two are easily angered.

One has mild social difficulties, occasionally being unintentionally rude. Three have negative mood problems. One still has problems concentrating, and another is immature for his age. One has convictions for violence and is held in a secure institution. Another has erratic mood swings, and is in hospital on a psychiatric ward.

“Has coped well with his condition but still gets very angry very quickly, but maturity has helped him deal with this.”

“I’m not moody. I like things in order. I hate people who lie. I get upset and can’t cope if I think I’ve let people down.”

As fathers

Men with XYY are fertile and do not run a risk of having children with a sex chromosome disorder that is discernibly higher than other men. The extra Y chromosome is generally lost when sperm are formed, and although a tiny fraction of sperm cells with a double Y or an XY constitution do slip through, this can also happen to men with XY chromosomes. There is no real evidence either that men with XYY are any more likely to have children with other chromosome disorders than other men.

A recent study of adults diagnosed after birth showed that they had fewer children, and their children were born when they were older than other men (Stockholm 2012).

Genes

The Y chromosome contains a gene called *SHOX*, which is also present on the X chromosome. This gene is known to control growth and it is thought that the extra copy of this gene is what leads to the increased height seen in boys and men with XYY.

Recent imaging studies have found greater brain volume with differences in the amount of white and grey matter in certain regions. In particular they found differences in an area called the prefrontal cortex that has a role in language and motor functions. The authors think that these differences may underlie some of the speech, language and behaviour differences seen in some boys and men with XYY. Research has suggested that the extra copy of a gene called *Neurologigin (NLGN4Y)* on the extra Y chromosome might be responsible for this. The *Neurologigin* gene produces a protein that helps cells stick to one another and is thought to play a role in forming connections between cells in the brain (Ottesen 2010; Bishop 2011).

Support and Information



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Join Unique for family links, information and support.

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Facebook groups

XYY Chromosome Disorder <https://www.facebook.com/groups/31905218415>

47XYY syndrome support group <https://www.facebook.com/groups/1406286052987882>

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This updated information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. The guide was compiled by Unique and reviewed by Professor Judith Ross, Department of Pediatrics, Thomas Jefferson University, Philadelphia, USA, and by Professor Dorothy Bishop, Professor of Developmental Neuropsychology, University of Oxford, UK 2014 (PM)

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