22q11.2 Deletion syndrome: What nurses need to know

The chromosomal condition 22qDS encompasses diverse complex medical, developmental, and mental health problems. Here is what the latest research tells us

In 1965, Dr Max Cooper addressed the US Society for Pediatric Research to share experimental proof 'that the lymphoid system is composed of two distinct cell populations' (Stafford, 2009). In the audience, paediatric endocrinologist Dr Angelo DiGeorge (1921–2009) realised that Cooper's evidence explained the absence of cellular immunity despite the presence of antibody-producing cells in three athymic children whom DiGeorge had attended at Philadelphia's St Christopher's Hospital. In 1967, the DiGeorge syndrome entered the medical lexicon (Lischner et al, 1967). More widely known as 22q11.2 Deletion syndrome (22qDS), it is the most common chromosomal condition after Down syndrome.

Clinical Aspects

Dr Suzanne Kelleher is a consultant general paediatrician working at Ireland's largest acute paediatric hospital – Children's Health Ireland, Crumlin – and in 2017 she established the national 22qDS clinic for children.

Dr Kelleher told *Practice Nursing* that 22qDS encompasses diverse complex medical, developmental, and mental health problems, with a prevalence of between 1 in 2000 and 1 in 4000 live births. 'Given Ireland's current birthrate of just under 60,000 births there should be 15 to 30 babies born annually,' she says, 'yet based on the current population attending the 22qDS clinic it's likely that many children remain undiagnosed.' Children born with 22qDS-associated congenital anomalies, like cardiac problems and cleft palate, are usually diagnosed in infancy, says Dr Kelleher. 'However, there is a cohort of children who may present to their GP with, for instance, chronic constipation, anxiety, recurrent infections, scoliosis, or poor growth; their dentist (enamel hypoplasia, delayed eruption of dentition, severe dental caries); primary care therapist (speech delay, autistic features, ADHD); or may struggle at school (social anxiety, specific and generalised learning difficulties). These represent opportunities to refer for assessment and genetic testing but may not be considered.'

Óskarsdóttir et al (2023) and Boot et al (2023) have recently published updated recommendations for managing children and adults, respectively, with 22qDS, which should provide helpful guidance for those in primary care.

Parental experience

Dr Kelleher's observations are echoed across the Irish Sea by Midlands-based Julie Wootton, who founded the charity Max Appeal (Max Appeal) in 1999 and is Chair of its Board of Trustees. 'My son Max,' says Julie, 'was born in November 1998 with catastrophic heart defects and a poor immune system, and he was rapidly diagnosed with 22qDS. With little known about this condition, internet searches led me to the Children's Hospital of Philadelphia.' Julie was soon sharing information with other families at Birmingham Children's Hospital, but when Max died of septicaemia in March 1999, Julie set up a support group and it was soon receiving telephone calls from within the UK and abroad. Max Appeal was quickly established.

Áine Lawlor was diagnosed with 22qDS when she was fifteen, and Áine's mother Anne Lawlor – Chair of the 22q11 Ireland Support Group (22q11ireland.org) – observes: 'As a mother, 22qDS means a different maternal journey: Áine will always need supervisory care that I'll need to provide until I no longer can. I co-founded 22q Ireland in 2007 because we needed charity status to fundraise and undertake research. Nobody else would undertake the work needed for our families and I had to find my tribe.'

Both Wooton and Lawlor emphasise an important point about so-called rare diseases like 22qDS: 'While rare diseases are indeed individually rare, they're collectively common,' says Lawlor, 'with over 10,000 rare diseases affecting one in 17. Genetic screening at birth is vital.' Wooton agrees, explaining that at Max Appeal 'we're campaigning for 22qDS to be added to the list of conditions screened through heel-prick tests of newborns.

Aside from their dedicated fundraising efforts, Wootton and Lawlor's respective charities' websites share an intellectual rigour and a determination that an evidence-based approach should be central to addressing the challenges of 22qDS, both for patients and their families. For example, Max Appeal has made available a recent paper by Chawner et al (2023) whose Cardiff-based exploratory study of 32 children with 22qDS found that '[m]otor and sleep function appear to be markers of early neurodevelopmental and psychiatric liability in 22qDS and thus may represent early targets for intervention.' Also, Max Appeal's National Consensus on the Diagnosis and Management of 22qDS (Max Appeal, 2023), notes Wootton, 'was written by professionals for professionals, explaining symptoms, regular checks and a life-long care pathway.'

An Irish study by O'Donoghue et al (2023) reported little empathy and scant awareness of 22qDS among healthcare professionals; that mental health is a particular concern among those participants with 22qDS interviewed; and that conferences provide parents with their main sources of information about 22qDS. This last point is particularly

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relevant, given that in November 2023 Dublin hosted the 5th European Conference on 22qDS, which featured over 20 speakers.

Patient experience

While Julie Wootton and Anne Lawler have provided much of the impetus behind enhancing awareness of 22qDS and other rare – that is, collectively common – conditions, patients have also been driving change. For example, Anne Lawlor and colleagues describe how a patient-driven innovation involving the 22q11 Ireland Support Group sought funding and political support to develop a multidisciplinary networked model of integrated care, a model which 'could act as an exemplar for other rare complex disorders and improve support to community-based primary care teams in managing these conditions' (Lawlor et al, 2017).

Another patient/researcher collaboration was co-authored by Áine Lawlor, one of six young women with 22qDS aged 21 to 35 years recruited to a 'Young Experts by Experience Panel' to assert that '[t]he lived experience of young people with chronic disease has seldom been heard in health research despite the clear policy imperative to hear the voices of children and young people as service users and rights holders' (Kerin et al, 2017).

In the context of lived experience, Julie Wootton makes the point that 'in the UK Parliament there has recently been a Private Members' Bill for Down syndrome, where it is described as a learning disability for which there are on-going resources. However, 22qDS is described as a learning difficulty, which implies that it could possibly be overcome. This is not the case.' And Anne Lawlor emphasises the need to hear the lived experience of families: 'Our "experiential knowledge" cannot be acquired by just reading about 22qDS. We know our own children best and we are their voices until such a time that they – hopefully – can find their own.' Lawlor also highlights the challenge of the relative 'invisibility' of the disability of 22qDS: 'When we meet a person with Down syndrome, we often underestimate their abilities whereas when we meet a person with 22qDS their abilities are often overestimated.'

And while acknowledging that children with 22qDS generally have a normal appearance and are not as easily identifiable as trisomy 21 (Down syndrome), Dr Kelleher notes that 'awareness of 22qDS is increasing among general paediatricians in Ireland, and 'ideally all children when diagnosed should be linked with the 22qDS clinic in CHI, where there is access to the 22q Complex Care Co-ordinator.'

Following the establishment of the CHI clinic in October 2017, 17 children were assessed in the first six months; the attendance rate was 94% and 29% of this group had their appointment co-ordinated with another specialist on the same day; and 46 children were seen up to January 2019 (McCormack et al, 2019). Report co-author Dr Kelleher points out that their study identified multiple areas of unmet need with reference to best practice guidance in this dedicated clinic, and 'It is hoped that we can improve care co-ordination further by engaging other specialists to run clinics on the same day, appoint a nurse specialist and adopt a clear care pathway, tailored to the Irish healthcare system using a life course approach to ensure the regular monitoring and anticipation of issues and early intervention that helps in maintaining health, well-being and quality of life' (McCormack et al, 2019).

Integrated care

Confirming precisely how patient/parent/healthcare professional collaboration can effect change, Wesley Mulcahy is Clinical Specialist Occupational Therapist at CHI, Crumlin, Ireland, where he is the National Care Co-ordinator for young people with 22qDS. Mulcahy's post arose 'through the efforts of young people with 22qDS and their families, following research showing that care for those with 22qDS was fragmented and stressful both to patients and their families. A business case was submitted to Ireland's Health Service Executive to use 22q as an exemplar condition for a care coordinator, and approved, providing a novel approach to meeting the needs of a rare disease population by having a single point of contact supporting integrated care.'

The concept of integrated care is evolving, says Mulcahy: 'I undertake medical and functional assessments with a consultant paediatrician, ensuring complex needs are captured and addressed. I also design a model of care for young people with rare disease; one that is transferable across other diseases, and which includes delivering parental and patient education, parenting support, developmental input, data collection, and advocacy across multiple agencies.'

Having been in post for two years, Mulcahy relishes the opportunity to be involved in creating something innovative: 'It's an example of a model of care in rare diseases that has never been done and could be repeated across other populations. I can contribute to something that will last long after I am gone from the post, and it allows me to bring together multiple stakeholders with a shared vision: improving how young people with 22qDS access and experience health services.'

22qDS and primary care

What improvements in the integrated care sector would enhance both the working lives of those like Wesley Mulcahy and the lives of their patients? 'To say "more resources" may sound like the lazy answer,' observes Mulcahy, 'but coordinating care provides unique insight into the gaps, and unfortunately the gaps are significant. In rare diseases like 22qDS, young people need to access acute care, primary care, Childrens Disability Network Teams, Child and Adolescent Mental Health Services, and also their communities – school, clubs, sporting groups.

A better awareness and knowledge of the impact across healthcare providers and the general population would have a positive effect on young people's social integration and take the pressure off performance components that

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they find difficult, secondary to their genetic disorder. A data coordinator would allow me to capture the clinical outcomes, positive or otherwise, and shape the model to best ensure it's meeting the needs of the young people who use it. Data and research would propel our understanding of this condition forward, thus shaping the services we create to meet these complex needs.'

Mulcahy's main message for primary care is that '22qDS is a lifelong and multi-system condition and it is likely that a 22qDS patient will have had multiple appointments across diverse health settings and involving a constant re-telling of their complex medical story, and it is still difficult each time.'

And Julie Wootton points out that for those in primary care, 'Being on the front line for patients puts nurses and allied health care providers in a unique position. It can take just one alert, vigilant, and motivated person to change the course of the life of someone with 22qDS.' An often-used phrase, adds Wootton, is the diagnostic odyssey, 'and this is certainly true for people with 22qDS, often referred to as the most commonly undiagnosed genetic condition or the most common genetic condition you won't have heard of.' The main features at birth that prompt genetic testing are generally a heart defect, low calcium concentrations and typical facial features, explains Wootton, yet 'only around half of those with 22qDS have a heart defect. So poor weight gain, feeding difficulties, developmental delay, nasal regurgitation and/or reflux, and repeated infections should trigger some bells'.

22qDS and school

In pre-schoolers, says Wootton, 'hyper-nasal speech is common and developmental delays become more marked, and in school-aged children poor memory retention and inability to socialise with peers, plus the ongoing battle with repeated infections and longer recovery times, often affecting attendance, are generally reported. However, schools often take the view that in time these children will catch up. The reality is quite the reverse.' And in the first study measuring executive function (EF) in 44 pre-school children with 22qDS, Everaert et al (2023) found that EF impairments were already present in early childhood, and as in previous studies among older children with 22qDS, congenital heart defects did not appear to influence EF performance, and the authors' findings 'might have important implications for early intervention and support the improvement of prognostic accuracy.'

And teenagers with 22qDS, adds Wootton, 'show behavioural problems more than their peers, often displaying autistic traits and this diagnosis can be helpful as schools have measures generally well in place, but attention deficit without hyperactivity often flies under the radar. It is around this time that more serious mental health issues emerge.' And schizophrenia, notes Wootton, 'affects around 25% of people with 22qDS – as opposed to 1% of the general population – together with other conditions like phobias and obstructive defiance disorder.

Finally

Wootton, Lawlor, Kelleher and Mulcahy in their own ways have been – and continue to be – effective agents for change as advocates for those living with 22qDS, either as patients or families. Julie Wooton is chair of The Children's Heart Federation, treasurer for Cardiovascular Care Partnership-UK (the patient arm of the British Cardiovascular Society), sits on the board of the European 22q Network, and runs the UK's All-Party Parliamentary Group for 22qDS. And Anne Lawlor was co-winner of the Unsung Hero Award 2022 at the Biennial International 22qDS Conference in Croatia.

With such inspirational efforts being undertaken and progress being made, one might reasonably expect that individually rare yet collectively common conditions like 22qDS will attract increasing – and well-deserved – attention among health professionals, including those working in primary care. **PN**

Boot E, Óskarsdóttir S, Loo JCY, et al. Updated clinical practice recommendations for managing adults with 22q11.2 deletion syndrome. Genet Med. 2023;25(3):100344. https://doi.org/10.1016/j.gim.2022.11.012

Chawner SJRA, Paine AL, Dunn MJ, et al. Neurodevelopmental dimensional assessment of young children at high genomic risk of neuropsychiatric conditions. JCPP Adv. 2023; e12162. https://doi.org/10.1002/jcv2.12162

Everaert E, Vorstman JAS, Selten IS, et al. Executive functioning in preschoolers with 22q11.2 deletion syndrome and the impact of congenital heart defects. J Neurodev Disord. 2023; 15:15. https://doi.org/10.1186/s11689-023-09484-y

Kerin L, McNicholas F, Lawlor A. Hearing the lived experience of young women with a rare genetic disorder 22q11.2DS regarding integrated care. Int J Integr Care. 2017; 17(5): A227, pp. 1–8. https://doi.org/10.5334/ijic.3537

Lawlor A, Kerin L, Orr D, et al. Developing integrated care in the context of rare chromosomal conditions: 22q11 Deletion Syndrome; A parent/clinician collaboration. Int J Integr Care. 2017;17(5): A215. https://doi.org/10.5334/ijic.3525

Max Appeal. Consensus Document. Consensus Document — Max Appeal (accessed 31 October 2023)

McCormack S, Orr D, McNicholas F, et al. Integrated care for 22q11 deletion syndrome in Ireland: Meeting children's needs through enhanced care co-ordination. Arch Dis Child. 2019;104(Suppl 3): A1–A428. https://doi.org/10.1136/archdischild-2019-epa.172

Óskarsdóttir S, Boot E, Crowley TB, et al. Updated clinical practice recommendations for managing children with 22q11.2 deletion syndrome. Genet Med. 2023; 25: 100338. https://doi.org/10.1016/j.gim.2022.11.006

Lischner H, Punnett H, DiGeorge A. Lymphocytes in Congenital Absence of the Thymus. Nature. 1967; 214: 580–582. https://doi.org/10.1038/214580a0

O'Donoghue E, McAllister M, Rizzo R. The experiences of families receiving a diagnosis of 22q11.2 deletion syndrome in Ireland. J Genet Couns. 2023; 32:618–634. https://doi.org/10.1002/jgc4.1667

Stafford N. Angelo M DiGeorge. BMJ. 2009; 339: 5379. https://doi.org/10.1136/bmj.b5379

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