The Impact of Family Advocacy Networks on Creating Partnerships and Improving Care of Rare Chromosomal Disorders; the Chromosome 22 Central Journey

*"Our daughter was born in 1976 and diagnosed with Cat Eye syndrome, a rare chromosome translocation. This was well before information in electronic or print format was available to us and to her medical team. Our youngest daughter actually found Chromosome 22 Central online and felt like her sister's needs were much more closely related to Emanuel Syndrome (ES) than Cat Eye. This information led to a conversation with our geneticist who confirmed her suspicions. The C22C connection has not only been a source of support for our family but also an opportunity to celebrate the successes and share in the difficult times of other children, youth, adults, and families living with ES. As I read the posts on Facebook, I am continuously struck by how genuinely connected the families are with each other and how information and support readily flow. It feels like home when you don't have to 'explain' your child to others including some of our own family members!" **

Advocacy networks and organizations have been active in the realm of health and disease for decades. The influence and role of these organizations in information sharing, research, and raising awareness raising has long been recognized (Dunkle et al, 2010). This article describes the journey and achievements of a parent-run support network for rare chromosome 22 disorders, particularly Emanuel Syndrome, that defied the odds to establish itself as a key advocate and expert for chromosome 22 disorders. The case study of this family-run support network will help illustrate the long-reaching positive impact of such an organization on support, awareness, research, advocacy, and ultimately, the field of healthcare.

Chromosome 22 Central

Established in 1996 with just 17 families, and initially named the International 11;22 Translocation Network, Chromosome 22 Central (C22C) is a parent-run support network focused on chromosome 22 disorders. Twenty-five years later, the organization links and supports nearly 4,000 families globally via social media and email, with close to 25% of the families being outside of North America (Chromosome 22 Central, 2021). The families all have one thing in common; the desire to support a family member with a rare chromosome 22 disorder.

The second smallest chromosome in the human body, the 22nd chromosome was the first human chromosome to be sequenced, paving the way for identification of related genetic disorders (Dunham et al., 1999). In simplest terms, deletions, duplications, or translocations on this chromosome can result in several disorders, with varied manifestations. For families affected by such disorders, the challenges are manifold. Useful information is almost as hard to find as it is to locate an expert on chromosome 22 disorders. Moreover, expert medical advice is only one aspect of the support needed, as raising a child with a rare disorder is often a lonely and challenging experience.

The loneliness, helplessness, and responsibility of round-the-clock care can be overwhelming for parents and families, and peer support from others in similar circumstances helps and benefits most families to face this challenge (Baumbusch et al., 2018). Though healthcare facilities and organizations frequently organize support groups, often families take the initiative and take ownership of their own organised rare disease networks. These initiatives frequently emerge as the leading source of information for most families (Limb, Nutt & Sen, 2010). C22C was also started as such a network.

While C22C was initiated as a network for families who had children with the unbalanced 11;22 translocation, now known as Emanuel Syndrome, it has since grown to include members affected by any of the chromosome 22 disorders. However, through the years the philosophy of C22C continues to be to support and guide families of children with any rare disorder primarily by providing them direction and by referring them to other relevant peer support groups.

'Together'

Stephanie Rese, founder of C22C, commenced the groundwork that would form the initial building blocks of the organization after her daughter Maia, born in March 1995, was diagnosed with an unbalanced 11;22 translocation. In her quest to find children like Maia and learn more about this rare disorder, Stephanie contacted and wrote multiple letters to parents' groups, families, and hospitals. She also connected with Dr. Beverly Emanuel, a geneticist from the Children's Hospital of Philadelphia who had been researching the 11;22 translocation for decades. Dr. Emanuel's research proved to be ground-breaking for the disorder that was later named for her.

By 1996, long before the days of Facebook and Instagram, Stephanie had realized there needed to be a medium to stay in touch with the families she had linked with. Hence, she soon began sending out newsletters to the initial handful of 'member' families. The newsletter, titled 'Together', was an effort to connect and share experiences, medical advances, and research on the rare genetic disorder her daughter had. Fortunately for Stephanie, and the then International 11;22 Translocation Network, this was the dawn of the internet era, and a basic website of the network was later established the same year.

As the group grew, it welcomed many parents of children with other chromosome 22 disorders who were seeking information and support. Despite the varied diagnoses, the group soon realized there were more things in common than different: the shock of the initial diagnosis, the daily battles, the navigation of hospital visits and procedures, and the many questions health care providers did not have answers for. Clearly, the struggles were remarkably similar. Recognizing this natural connection and the common needs of all families, the network was retitled *Chromosome 22 Central*.

With the social media boom, C22C moved towards a largely internet-based presence with active Facebook groups and fielding of inquiries by email. Despite the currently large numbers, C22C remains a very close-knit network with founding members an email or telephone call away to provide quick and personalized responses.

"They are my second family who completely understand what I'm going through, and I can count on (them) when in need." (Chromosome 22 Central, 2021)

While initially started as a charity in Canada in 2002, the financial arm of the group runs solely out of the USA as a 501©(3) corporation.

The Vision

From its inception, C22C's vision has been to connect, support and advocate for chromosome 22 disorders with the goal of improving lives and giving hope to the children affected and their families. The vision of C22C has largely rested on the pillars of ***supporting families and knowledge sharing,*** and ***research assistance and advocacy***.

Family Support & Knowledge Sharing

Families lie at the heart of C22C. A recent C22C member engagement survey revealed that nearly 98% of C22C members are parents or families of individuals with a chromosome 22 disorder (Chromosome 22 Central, 2021). At its core, the organization has been a focal point for caregivers to reach out, connect and feel less isolated in their rare journeys. From telephone calls to exchanging letters and emails, the early years of C22C saw families telling their stories, sharing experiences, seeking information, and drawing strength and hope from each other. A grateful parent summed it up well in the survey;

"C22C has put me in touch with families in the same boat as us. Advice from those who have dealt with medical issues, surgeries, medications etc. My daughter is 39, there was no information available for me at that time. It is a lonely and sad time when you bring your child home and try to find your way when medical staff is not familiar with the syndrome. This group is the answer parents are needing at the time they need it the most." (Chromosome 22 Central, 2021)

The telephone calls, letter and emails were later supplemented by the quarterly newsletter. 'Together' was instrumental in connecting families internationally. Between 1996 to 2010, it kept parents updated on the most recent data on chromosome 22 disorders, links to resources, upcoming meeting alerts, research participation opportunities and information on new members. The network's close links with Dr. Emanuel proved valuable with regular updates coming in on her ground-breaking research on the 11;22 translocation. Additionally, the C22C website, established in 1996, offered information on chromosome 22 disorders, research links, and event notices. The current version of the website, which is presently being updated to be even more comprehensive, continues to be a hub for all chromosome 22 disorder-related information and resources, complemented by presence on social media; the significance of which cannot be overstated.

If the internet revolutionized human interaction, social media evolved and transformed it. C22C's social media presence has developed into an active community with open discussions, sharing of experiences and knowledge, asking questions, or just seeking comfort. To some parents it has been a place *"to contribute where I can, comfort where I can and share a laugh or two when possible"* while for others a way to learn *"how others cope with everyday life challenges - what has worked, what hasn't worked, (and) things to question"* (Chromosome 22 Central, 2021). The Facebook groups have taken the form of an online support group, which, like in-person support groups, provides the much-needed strength taken from others in similar circumstances (Plumridge et al., 2011). The C22C survey revealed that nearly one-third of members accessed C22C social media daily for information and support (Chromosome 22 Central, 2021).

Very recently, a mother wrote about her daughter's recent diagnosis of an exceedingly rare 22 deletion. While doctor consults and internet research had yielded next to nothing on the disorder, a post on the C22C Facebook group connected her with two parents whose children had the same deletion, and who provided support and recommendations for next steps. A long-time member of the group noted;

"There aren't adequate words. Finding support from people, who have been where we are and are where we are, has been incredible. The support from other parents has been immeasurable." (Chromosome 22 Central, 2021)

The support offered by C22C however is not limited to only online activity. Over the past twenty-five years, C22C has held several events; from small, organized meet-ups to bigger conferences bringing together researchers, multidisciplinary health professionals and families. For most families these have

been opportunities to learn more about the care of their child, interdisciplinary management and also, importantly, a chance to talk and meet others who understood their journey.

"I'm happy to know others who understand me and this life. It can be very lonely being a special needs parent. The connections are everything, being able to talk, laugh and or cry with someone has helped tremendously." (Chromosome 22 Central, 2021)

Advocacy and Research

Despite the family-centered focus of the network, the contribution to advocacy and research for chromosome 22 disorders has been significant. Stephanie's initial contact with Dr. Emanuel evolved from a personal connection to a long-lasting association between C22C and Dr. Emanuel's research team. The team's engagement with C22C has led to an ongoing collaboration in the 11;22 translocation research landscape. Stephanie and the network helped link the research team with families to collect patient blood samples for studies that were published in 2000 and 2001 (Kurahashi et al., 2000; Kurahashi & Emanuel, 2001). Furthermore, the network also linked researchers to families with other chromosome 22 disorders such as Cat Eye Syndrome and 22q11.2 Deletion Syndrome.

A landmark in the 11;22 translocation research landscape was a review study based on data collected from the largest cohort of individuals with Emanuel Syndrome via the C22C platform. In 2007, Stephanie was connected to the then medical genetics resident, Dr. Melissa Carter, at the Children's Hospital of Eastern Ontario, who in partnership with the network and Dr. Emanuel, led the review (Carter et al., 2009). This was the foremost publication detailing the natural history of individuals with this rare disorder including details on developmental and behavioural issues, and the abilities and capabilities of the children as they grow. Published in 2009, the article is considered a milestone for documenting the clinical spectrum of Emanuel Syndrome and closing a large data gap on the developmental arc and prognosis of this syndrome. Importantly, this was the first time the name Emanuel Syndrome was used in a scientific publication, Remarkably, the term Emanuel Syndrome was nonexistent only five years before the article was published; the name first took root during an advocacy event five years prior.

As part of its advocacy efforts, C22C co-hosted the World Congress on Chromosome Abnormalities in 2004 in San Antonio, Texas. The congress aimed to raise awareness and build connections amongst families, and other stakeholders. During the congress, many of the C22C members including Stephanie and Murney Rinholm, current President of C22C, discussed giving a 'name' to their children's condition. The discussion, followed by guidance from geneticists, prompted Stephanie to contact Dr. Victor McKusick, founder of the Online Mendelian Inheritance in Man (OMIM), an online catalogue of human genes and genetic disorders (OMIM, 2021). C22C advocated that the disorder that had been known by multiple names including Supernumerary Der (22) Syndrome or Partial Trisomy 11/22 due to unbalanced 11/22 translocation, be named after Dr. Emanuel to honour her extensive research work on the syndrome.

Owing to C22C efforts and Dr. McKusick's support, on November 18th, 2004 Emanuel Syndrome entered OMIM as *#609029* with a supplementary GeneReview entry by Dr. Emanuel herself, shortly thereafter (OMIM, 2004). This marked a significant milestone in the history of rare disease support networks, when a network successfully advocated for naming a rare chromosomal disorder. The name not only gave an identity to the rare disorder, but also granted validation to the hundreds of families affected by Emanuel Syndrome. The single identity also enabled caregivers, families, and health workers to access information on the disorder more easily. Emanuel Syndrome had certainly come a long way from the days when Stephanie had to struggle to find any information on the translocation and its clinical course.

Family Advocacy Groups and Health Professionals

The C22C story is a stellar example of how family-run advocacy groups or support networks can work with and support health professionals to help advance family support, research, and advocacy. This symbiotic relationship can prove to be an asset in the rare chromosomal disorder journey.

Engaging families is central when providing health care to a child, no matter what the health issue is (Kokorelias et al., 2019). For rare chromosomal disorders, the significance increases manifold. Families are the only constant in the lives of these children (Cardinali et all., 2019). As such, families are not only at the core of the care being given, but over time, also tend to have high levels of knowledge concerning diagnosis, features, and management of the disorder (Jansen et al., 2017). This knowledge, together with the experiences of day-to-day life, not only benefits other families seeking answers, but also delivers crucial support to health care providers.

Evidence indicates that a rare disorder diagnosis is inherently a risk factor for sub-optimal health care. In their qualitative study, Grut and Kvam (2013) concluded that most healthcare providers are hesitant to be proactively involved in management of an 'unknown' condition given lack of experience with the disorder and the dearth of relevant information. This makes the role of family-run support networks for rare disorders all the more crucial given the value and relevance of individual lived experiences and experience-based knowledge (Alsema et al., 2017). In practice there will be many general practitioners, pediatricians, and allied heath care providers who may never have managed a child with a particular rare chromosomal disorder, and could benefit greatly from the practical experience found in such networks (Baumbusch et al., 2018), which has certainly been the case with C22C.

"There is very little information out (there), we have had such a hard time even with the doctors not being knowledgeable about this disorder and has caused some delays in some of the surgeries my child has had." (Chromosome 22 Central, 2021)

When it comes to rare disorders, advocacy networks such as C22C play a key linking and facilitating role between all the main stake holders – children, caregiver/families, health care providers and researchers – in a mutually beneficial and multifaceted way, an overview of which is presented in Figure 1. Although it would be unwise to generalize the C22C experience to all rare disease support networks, many aspects can be representative of and apply to rare disease networks globally.

Informational and Mental Health Support: Supporting families, while apparently only of benefit to families, indirectly support healthcare providers as well. Families receive informational and emotional support from advocacy networks, thus, taking on some of the responsibilities of healthcare systems. Additionally, several vulnerable families in different geographic locations are unable to access support from their healthcare systems – for them, the possibility to reach out to an online network is invaluable. In the C22C engagement survey, nearly 63% of the respondents identified 'asking questions' from other members as a key reason for joining the network. A member living outside North America noted:

"(C22C) Was my lifeline when my son was diagnosed. (There) Was no other information or groups in this country." (Chromosome 22 Central, 2021)

"If we did not have this information, we would have struggled even harder, as our daughter's diagnosis is not so known here. (After connecting with C22C) we could help guide the doctors." (Chromosome 22 Central, 2021)

Most rare disorder caregivers experience shock, helplessness, frustration, and crave emotional support (Glenn, 2015). Finding that support through understanding and shared emotions from someone in similar circumstances is unmatched (Cardinali et all., 2019). Many who felt isolated and confused, found that support with family support networks such as C22C.

"We were told we were alone in the beginning…and knowing there were others that experienced what we had or could relate to our experience was just so amazing. I can never express the comfort and calming spirit this gave us." (Chromosome 22 Central, 2021)

Facilitating Research: Rare disease evidence is often marred by data gaps. While caregivers are eager for updated evidence to support diagnosis and management, researchers are keen to advance their research and investigation (Forsythe et al., 2014). Yet, there are several barriers to address. Rare disease advocacy networks can support researchers in several ways including helping to secure funds, collect data, and disseminate findings (Landy et al, 2012). In addition, seeking and accessing families with rare chromosomal disorders who are willing and able to collaborate for research purposes, is not an easy task

for genetic researchers. Privacy laws and the inability to contact families without a referral remains a barrier. Advocacy networks such as C22C play an integral role in recruiting research subjects. The Carter et. al. (2009) research paper stands out as an example. The study was based on C22C connections with families and the data that Stephanie collected via questionnaires.

Families may not be able to fix their loved one's rare chromosomal disorder, but they can participate in life-changing research which can provide invaluable information to guide management. A systematic review of 35 rare disease studies estimated that nearly half of the studies had engaged with patient organizations to access participants (Forsythe et al., 2014).

Building Bridges: Often, families with a recent diagnosis will not have all their information needs, regarding relevant experts and services, met (Baumbusch et al., 2018; Alsem et al.,2016). It can take an army of experts and professionals to help a child with a rare chromosomal disorder to thrive and grow to potential. In many instances, healthcare providers will lack knowledge or overlook providing information on how best to access current and future services. A survey of more than 100 parents, of children with profound intellectual and multiple disabilities, showed that nearly a quarter were not provided information on supportive services by their healthcare providers (Jansen et al., 2017). Family support networks, however, have a system to readily provide this information to family and healthcare providers, thus building bridges and linking the newly diagnosed families with experts. Conversely, care providers can build bridges by introducing patients and their families to the advocacy and support networks who can best provide support in many forms.

"C22C families helped get the right medical care, the right therapies and the right resources for school and community. I would have been lost without them." (Chromosome 22 Central, 2021)

Education and Experience Sharing: Knowledge sharing by advocacy and support networks is not limited to families. Substantial information and experiences are shared through conferences, meet-ups, newsletters, and media with the healthcare community and the public (Cody, 2006). With the large number of rare chromosomal disorders that have been discovered, it is impossible for healthcare providers to have all the answers to medical queries or be aware of all latest research. Further, the research and information on rare disorders is relatively limited. Thus, dedicated networks can potentially be 'one-stop' repositories for families as well as healthcare providers to access updated research and information. As research has identified, being part of support groups and gaining information empowered most caregivers, enhanced communication and encouraged a collaborative relationship with healthcare professionals (Bartlett and Coulson, 2011; Dudding- Byth, 2015). Families linked with C22C often describe how they updated physicians on new research or care techniques. As further evidence that family networks are often the experts, it is not uncommon for C22C family members to report that medical professionals have provided them with the results of research into their child's disorder taken directly from the C22C website. A C22C family commented:

"We would have been so lost, (but after connecting with C22C) knew what to expect going forward and shared so much info with physicians." (Chromosome 22 Central, 2021)

Advocacy: Rare disease advocacy is not easy. Numbers are few, funders are hard to engage, and policymakers are largely unaware or indifferent (Pai et al., 2019). Rare chromosomal disorders often do not get the recognition or hype as high-profile and common conditions (Cody, 2006; Pai et al., 2019). Rare disorder advocacy networks can be instrumental in drawing attention to the issue, collating research, developing resources, engaging multisectoral partners and most importantly, initiating change.

The collective advocacy of family-run support networks can influence communities and change perceptions while enhancing health care provider and policy makers' awareness. As a renowned Canadian child disability advocate Rachel Martens described, *"Lived experience carries such strong potential for impact on high-level policy" (*Rachel Martens, personal communication, 10th March 2021).

Conclusion

The journey of families of children with rare chromosomal disorders is unique. It takes a team of health care professionals to help families navigate this journey; geneticists, obstetricians, pediatricians, multiple specialist physicians, occupational therapists, physiotherapists, surgeons, social workers and so many more. However, the C22C experience demonstrates that the role of parents and family advocacy networks is invaluable, relevant and, in most cases, underestimated. Our recommendation would be for healthcare providers to engage with family advocacy networks to enhance the care being provided to those affected by rare chromosomal disorders. Networks like C22C may not have all the answers; but they can surely help to find them, not only for the families, but also for all the other stakeholders treating or researching these rare disorders.

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