GENE PEOPLE

the genetic conditions support network

Major Conditions Strategy consultation response

Who this response is from

Gene People is a charity providing support and information to people living with genetic conditions, their families and carers, and to the condition-specific support groups that work with specific communities. We receive approximately 200 enquiries to our unique genetic counsellor-led helpline each year, and currently have over 140 support groups in our free to join Partnership Network.

Gene People is sending this narrative response to the Major Conditions Strategy on behalf of the genetic conditions' community which we serve. The majority of the individuals that contact Gene People for support are concerned about the rarer genetic conditions, and it is that which has informed our response.

While the consultation is for the Major Conditions Strategy, we want to ensure that the rare conditions that fall within each category of major conditions are not forgotten, and that the Strategy has solid referral pathways for conditions that need specialist diagnosis routes, such as genetic testing.

The rare disease context

We have provided the rare disease context in previous consultation responses and include some topline statistics for completeness.

There are approximately 3.5 million people affected by rare conditions in the UK[i], which means many more people from their wider families are involved in caring for and supporting them.

Estimates of the numbers of rare diseases have, until recently, suggested that there are around 7,000 conditions. Rare-X have published a report that posits that the number of rare diseases exceeds 10,000[ii], suggesting a considerable amount of mis- and under-diagnosis. Approximately 80% of rare conditions have a genetic cause. Very few conditions are screened for currently. This is changing with projects like the 100,000 Genomes Project and the forthcoming Newborn Screening Study.

Most rare conditions begin to present symptoms in childhood, with a significant proportion of those conditions (more than 30%[iii]) resulting in the death of a child before their fifth birthday. There are treatments for approximately 5% of rare conditions.

Having a family member with a rare condition can cause several social determinants of health inequalities, such as poverty, issues with employment, educational attainment, and housing[iv]. Having a rare disease in a family is itself a health inequality, given the lack of services and understanding for these conditions.

Condition specific support group landscape and services

The UK is fortunate in that there is a well-established voluntary sector, which means that voluntary groups and charities can be formed to support those with rare conditions. It is estimated that there are 300 formal groups with additional informal

groups through social media[v]. Some conditions do not have patient organisations but are a loose collective of affected individuals, perhaps global in reach due to the low number of patients.

These groups can be wholly volunteer-led and run, or highly developed charities. It is important to recognise that each are expert in their own condition; it is not feasible for a group with a small patient population to grow to the size of a charity serving the general population, such as Cancer Research UK. It is equally important to recognise that some major condition charities include the rarer forms of their conditions in their work.

Patient groups and organisations can offer a wide range of services, including peer support, trained adviser support and advocacy, information materials, and opportunities to meet others in the same situation through virtual and in-person events. Some may offer specific services to siblings, bereaved parents jointly, or parents in peer groups.

These groups are funded in a variety of ways from public donations and fundraising, corporate support, and potentially contracts for supplying services. There is no set rule as to where funding is from, which can create sustainability issues. It is well-documented that charities are suffering from declining income given the cost of living crisis impacting donations from individuals and grants from trusts as endowments are impacted by the general economy. In addition, charities are facing increased rental and utility prices, and, where they have paid staff, may be having to increase salaries in order to retain staff given the current crisis. These factors are making the voluntary sector increasingly volatile and the number of charity closures[vi] is anticipated to increase. This applies to those working with communities affected by health conditions, jeopardising the support available.

The relationship between Major Conditions and Rare Diseases
We want to emphasise the relationship between Major Conditions and Rare Diseases, therefore, give examples of conditions for each category.

- ***Cancers***

There are a number of rare hereditary cancer syndromes, many are likely underdiagnosed. For an overview see: https://www.cancerresearchuk.org/about-cancer/causes-of-cancer/inherited-cancer-genes-and-increased-cancer-risk/inherited-genes-and-cancer-types

Li-Fraumeni syndrome (LFS) is an inherited condition that is characterized by an increased risk for certain types of cancer. Affected people often develop cancer at an earlier age than expected and may be diagnosed with more than one cancer during their lifetime. LFS is primarily associated with sarcomas (cancers of muscle, bone or connective tissue), breast cancer, brain tumours, leukaemia and adrenocortical carcinoma; however, many other types of cancer have been reported in people with this condition. It is typically caused by changes in the TP53 gene and is inherited in an autosomal dominant manner.

Prevalence: 1 in 5000-20,000 families

Birt-Hogg-Dubé (BHD) syndrome is an inherited condition, characterised by the development of fibrofolliculomas (benign skin tumours), pulmonary cysts and pneumothorax (collapsed lung), and predisposition to kidney cancers.

Prevalence: 600 families worldwide

- ***Cardiovascular disease, including stroke and diabetes***

Cadasil syndrome - CADASIL (Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy) is an inherited disease of the blood vessels that occurs when the thickening of blood vessel walls blocks the flow of blood to the brain. The disease primarily affects the small blood vessels in the white matter of the brain. CADASIL is characterized by migraine headaches and multiple strokes, which progresses to dementia. Other symptoms include white matter lesions throughout the brain, cognitive deterioration, seizures, vision problems, and psychiatric problems such as severe depression and changes in behaviour and personality. Individuals may also be at higher risk of heart attack. Some individuals may not show signs of the disease until later in life. CADASIL is caused by a variant (or genetic change) in a gene called NOTCH3. Inheritance is autosomal dominant.

Prevalence: 1 in 50,000

Brugada syndrome is a heart condition that causes a disruption of the normal rhythm in the heart's lower chambers (ventricular arrhythmia). Signs and symptoms usually develop in adulthood, but the diagnosis may be made at any age. Symptoms and complications often occur during rest or sleep, and may include fainting, seizures, difficulty breathing, or sudden death. The underlying genetic cause of inherited forms of Brugada syndrome is not known in most cases, but in up to 20-30% of people with Brugada syndrome, it is caused by a genetic change in the SCN5A gene. A number of other genes have been reported to be associated with Brugada syndrome in the literature, but the role they play in causing Brugada syndrome remains to be clearly defined. The genetic form of Brugada syndrome typically is inherited in an autosomal dominant manner.

Prevalence: 1-5 in 10,000

- ***Chronic respiratory diseases***

Pulmonary Fibrosis and/or Bone Marrow Failure Syndrome, Telomere-related, 1 (PFBMFT1) is an autosomal dominant disorder characterized by the onset of progressive pulmonary fibrosis in adulthood. Some affected individuals have signs of bone marrow failure, such as thrombocytopenia, or liver dysfunction, including hepatopulmonary syndrome. Other features of dyskeratosis congenita, including premature graying of the hair, may be observed. Telomeres are shortened compared to controls.

Prevalence: 1 to 5 out of every 1 million people.

Primary ciliary dyskinesia (PCD) is a rare, inherited (passed down through the family), condition that affects several organs and gets worse over time. Children with PCD have a problem with mucus build-up, which leads to inflammation in the airways and infections in the lungs, nose, sinuses and ears. Children with PCD have the condition all their lives.

According to PCD Support UK, PCD affects 1 in 15,000 people in the UK.

- ***Dementia***

Fahr Disease described in 1930 by T. Fahr is a genetic (inherited) neurological disorder characterized by abnormal deposits of calcium in certain of areas of the brain (including the basal ganglia and the cerebral cortex).

Prevalence: less than one case per million

Fronto Temporal Dementias (FTD) are a group of neurodegenerative disorders associated with shrinking of the frontal and temporal anterior lobes of the brain. Symptoms include marked changes in social behaviour and personality, and/or problems with language. People with behaviour changes may have disinhibition (with socially inappropriate behaviour), apathy and loss of empathy, hyperorality (eating excessive amounts of food or attempting to consume inedible things), agitation, compulsive behaviour, and various other changes. Examples of problems with language include difficulty speaking or understanding speech. Some people with FTD also develop a motor syndrome such as parkinsonism or motor neuron disease (which may be associated with various additional symptoms). There is a strong genetic component to FTDs. It sometimes follows an autosomal dominant inheritance pattern, or sometimes there is a general family history of dementia or psychiatric disorders. The three main genes responsible for familial FTD are MAPT, GRN, and C9orf72. However, the genetic cause of familial FTD cannot always be identified.

Prevalence: 15-22 per /100,000 population

- ***Mental ill health***

Gene People sent a response to the Mental Health and Wellbeing plan consultation as part of a collaborative. The response is published on our website at https://genepeople.org.uk/about-us/national-policy/

- ***Musculoskeletal disorders***

Central core disease (CCD) is an inherited condition that involves muscle weakness, skeletal abnormalities, and an increased chance of having a severe reaction to some anaesthesia medications. Muscle weakness ranges from mild to severe and typically affects muscles in the trunk and upper legs, though muscles in the neck and face can also be affected. Skeletal abnormalities may include curving of the spine (scoliosis), dislocation of the hip, or restricted motion in certain joints (contractures). Some individuals with CCD have an increased chance of having a severe reaction to anaesthesia, called malignant hyperthermia, which may cause muscle rigidity or break-down (rhabdomyolysis), a high fever, or a rapid heartbeat. RYR1 is the only gene associated with CCD and clinical testing is available to look for disease-causing alterations in this gene.

Prevalence: 6 in 100,000

Acromesomelic dysplasia describes a group of extremely rare, inherited, progressive skeletal conditions that result in a particular form of short stature, called short-limb dwarfism. The short stature is the result of unusually short forearms and forelegs (mesomelia) and abnormal shortening of the bones in the hands and feet (acromelia). At birth, the hands and feet may appear abnormally short and broad. Over time, the apparent disproportion becomes even more obvious, especially during the first years of life. Additional features may include limited extension of the elbows and arms; progressive abnormal curvature of the spine; an enlarged head; and a slightly flattened midface. Acromesomelic dysplasia is inherited as an autosomal recessive trait. There are different types of Acromesomelic dysplasia, which are distinguished by their genetic cause.

Prevalence: less than 100 reported cases in the medical literature

Conclusion and Recommendations

We understand that the purpose of the Major Conditions Strategy is to improve service delivery for conditions that affect large numbers of people, however, Gene People asks that provision is made for those people whose condition is rare but falls within the categories stated. Our key recommendations are:

1) That the Strategy includes clear pathways to diagnosis for those whose conditions are not easily identified due to rarity
2) That consideration is given in the Strategy to signposting people living with a genetic condition to the relevant support groups swiftly following diagnosis.

In addition, we would like the recommendations made in our original response to the Mental Health and Wellbeing plan implemented.

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[i] https://www.gov.uk/government/publications/uk-rare-diseases-framework/the-uk-rare-diseases-framework

[ii] https://rare-x.org/blog/2022/06/07/rare-x-releases-new-report-that-uncovers-large-number-of-previously-uncounted-rare-diseases/

[iii] https://www.gov.uk/government/publications/uk-rare-diseases-framework/the-uk-rare-diseases-framework

[iv] https://www.health.org.uk/publications/reports/the-marmot-review-10-years-on?gclid=CjwKCAjwqauVBhBGEiwAXOepkaON3KNp93I5Se7nFcBvdE4blLa8aBEprm9_1QO4d7r75tqaMdOh7BoCwRoQAvD_BwE

[v] https://genepeople.org.uk/for-charities-and-patient-groups/genetic-disorder-charities-patient-groups/

[vi] https://www.civilsociety.co.uk/news/charity-closures-warned-as-inflation-exceeds-10-for-first-time-in-40-years.html