Online Resource 2 Free Responses

This supplemental information includes all participants' responses to this free response question: *If you would like to elaborate on any of the questions listed above and provide insight on your experiences as a female X-linked carrier, please do so below.*

The responses were evaluated by authors JC and LP and grouped into different categories corresponding to the study aims.

Aim 1: Carrier Status / Experience – Investigate X-linked carriers' experience with carrier identification.

For the first question; at what age do you feel a person should know if they are a carrier or not - I put 16 but I believe it should be as soon as birth. So many life choices it affects, not just their future parenthood.

I feel that a person should be told not at a certain age but when they are mentally able to understand or are sexually active. My 1st son was diagnosed in 1992, at that time things were not as well known. There is a lot of things I could say but my best advice is the sooner you find out the better. Newborn screening is the best thing.

I was adopted and thankfully my bio mom contacted the adoption agency to let me know, so before having children I was able to get tested and was a verified carrier.

The question about the age to know you are a carrier is extremely difficult to answer. Obviously, the ethics and burden of knowledge that our daughters are carriers is a weighted response.... I feel that they can have a childhood and long have to worry. Once they get to child-bearing years-I think it's vital for them to know what the risks are and what "it" all means.

As a child I was made aware of my carrier status. However, the belief was deeply rooted in our family that females were only carriers and that no progression to disease state would ensue. I was discouraged from telling medical providers about my X-linked disease because it "isn't a big deal" and also that they would not know what it was anyway. Worries of the disease and conversations initiated with my parents regarding reproductive options were hushed, thus limiting my knowledge well into adulthood. This was largely due to religious beliefs within the family unit. I did not fully understand the disease as it would affect me or my children until after I had 2 of my 3 children. While I did have another child after I was better informed, this was not planned. My first two children (one female, one male) are now affected with my third being unaffected. In a move to delineate from my parents' approach, I have chosen to initiate conversations with my children early and answer questions honestly. There will always be a channel for open communication in my home.

I had daughters. My elder daughter gave birth to 3 sons who inherited BCM.

I think carriers should be told as soon as they can understand the concept of being a carrier and what it will mean for future generations.

For the earlier question regarding the age in which someone should be notified about their carrier status I indicated 0. I do believe that newborn screening for x-linked diseases (in my case ALD) should be implemented across the country. Parents should have the right to 1) know their child potentially has a deadly disease so they can 2) make informed decisions about their health going forward and 3) can inform carriers when THEY are ready to have a conversation about reproduction. I may not have fully understood my carrier status when I was 11 however it did allow me to make informed decisions about future reproduction.

My mother, who is extremely symptomatic for ALD, was undiagnosed for many years, and then misdiagnosed before finally, after 20 years, correctly diagnosed as having ALD. My mother is of a generation who completely trusted her doctor and believed he had her best interest at heart, but after his insensitivity once she was correctly diagnosed with ALD, it's clear he had become bored with her "case" and symptoms. My daughter is a carrier and at

6 years old, knows of her carrier status. We discuss often, mostly in conjunction with her younger brother's ALD diagnosis, but I am confident that her knowledge from a young age will benefit her.

Aim 2: Access to Medical Information – Explore X-linked carriers' access to medical information such as potential symptoms and/or risks associated with being a carrier.

More information is needed so the medical community better understands the carrier status and the stress and worry it causes.

I donated so much of my blood for research they used my blood to create the test for prenatal. I used it 3 times. I actually met Dr Good who invented CGD. He was our second opinion. Doctors need to believe their patients when they tell them about x-linked carrier conditions. Like lupus, my face turns red every night, my cheeks turn red often during different situations. I suffer with migraines, pimples my liver is fatty my kidney has cyst I suffer with IBS. I don't drink I have very small choice of foods I eat. Never fast food but my point is my doctor doesn't seem to believe me. No smoking no drinking no drugs. I can't afford doctors. I really wasn't prepared for this.

I have a 46 year old son in a wheelchair. A daughter who is a carrier and has a son in a wheelchair and a daughter with many symptoms.

I hate the term carrier. When I found out I was a "carrier" I thought I, myself, would be ok.

I knew I was a carrier right away because of my dad's hemophilia. What I didn't know (none of us know) was that I could have it too. Doctors denied this for many years, resulting in no treatment for me until my joints were already very damaged from internal bleeding.

It is still so difficult to find someone who understands my disease and is able to help me. It is frustrating to get the care that I need.

I am struggling to find a doctor to discuss my symptoms and their association with my carrier status.

I feel that there is no concrete answer as to what is and isn't symptoms of ALD. That makes it difficult to advocate for yourself.

Many doctors have not believed me that carriers can have symptoms, the severity of symptoms, or that I could have symptoms at a younger age (31 now, but I believe I have had symptoms since at least mid 20s, and I've always had profound fatigue, even as a child).

I was incorrectly diagnosed from age 5 to age 40 when my daughter started having symptoms. She had biopsy that showed AS and then I had genetic testing done. No family history so I am considered spontaneous mutation. Had all the symptoms of AS including hearing loss but the MD never evaluated due to no family history.

The questions re having children are tough for me to answer correctly. I am 60 years old so those don't apply to me but I couldn't say that as an answer. My son had numerous hospitalizations for dehydration and despite me giving family history including a brother who died of Shilders disease I had 3 children and not the OB nor any doctor had a lightbulb go off. My mother was not told it was genetic and she was never told her troubles were due to her status. He died in the 1950s before I was born. My son was finally diagnosed with Addison's disease at age 7 then was told he had AMN. I reached out to the ULF and was told they couldn't know. This was 1991. We took him to see Dr Moser where he was diagnosed ALD. We were told to call Dr Krivit in MN about transplant. Our son was the 7gh in the US. Dr Krivit is the one who explained to me that my walking trouble was due to my ALD carrier status. I was too busy as most of the moms are taking care of their children to see about my troubles. Finally after my little girl asked my husband why I kept falling down I started trying to find help. I still feel even though I am fortunate to live near Boston and see Dr Eichler that over the years it was not taken seriously and now that I am almost wheelchair bound I feel I don't get heard. I ask about tremors and other symptoms not written anywhere and I guess I have things not many do. We don't even have our own name. We are diagnosed as AMN which is good at least it is recognized we do have disease but when a clinician looks up AMN and sees male it is very confusing. I would like

to see a name for us and our disease. I would like information regarding our disease available. Even ALD groups don't have information or correct information on their websites.

If there was more information and research I would not have watched my son die. Also as of now I feel lost and left out in the cold with no answers. If more information was out there is wouldn't be fearful for my daughter and niece's futures. Right now it feels like there are no answers.

I try to educate other medical providers (as a prior provider myself) but many do not care to learn about symptomatic carriers and continue to brush me off as "all in my head" when it comes to pain or other symptoms. Formal education or CME needs to include the changes in findings for x linked carriers and symptoms to be taken seriously.

I began having symptoms in my late 30s I started the quest to figure out a diagnosis when I was about 42. It took me 3 years to be diagnosed, seeing every specialist known to man. I was finally diagnosed by a resident at the UCI neuromuscular center. It baffles me that my original neurologist had no idea what my diagnosis was and that he wasn't even the one to refer me to a neuromuscular specialty center. I live in California and have to travel all the way to Boston annually to see Dr. Eichler because he is the only doctor that I've found to be knowledgeable about the disorder. I'm willing to do anything to slow my symptoms as they are progressing rapidly and I want to have a decent quality of life. Please let me know if there are any additional opportunities to be involved in studies or trials. I'm willing to try anything!

i am 56 & just now learning by looking on Facebook about carriers have symptoms. when my brother was diagnosed in 1980 and my son in 2001 no doctor has ever mentioned to me about ALD affecting my health. In fact back in 1970 they said males were affected and females were just carriers. I have RA but also other pain no one can explain, this may be it. I have tried to google but little information comes up.

I was diagnosed in 1996 when my 11 year old son (my oldest) was diagnosed with ALD. I had 4 children (3 boys and 1 daughter) at that time. I was pregnant with my 5th child, a son. All of my son's siblings were negative for ALD. He passed from complications related to a bone marrow transplant at Johns Hopkins in 2006. I began to experience symptoms in 2011, at age 51. I live in a rural community in the Midwest and there are no physicians in my community who are knowledgeable about ALD symptom management.

The biggest problem is that primary care doctors are so uneducated on Muscular Dystrophies, trying to explain the dystrophin gene and the carrier status it makes it very hard to move forward if you are not very knowledgeable and proactive.

Aim 3: Reproductive Options – Assess how carrier status affects reproductive plans and preferences for reproductive options.

ALD has affected my family since 1959 when my mother's brother died from ALD (then it was called Schilder's Disease). I lost both my older and younger brothers from ALD (in 1972 and 1979). I had my carrier test in 1987 when I was 18 years old. I terminated my first pregnancy at 5 months (a boy - diagnosed with ALD through amniocentesis). I gave birth to twin daughters in 1999. I did IVF with PGD. My daughters had their carrier tests when they turned 18 in 2017. One is a carrier and the other is not. I am an affected woman with ALD. My diagnosis came in November 2019. I am suffering with severe burning neuropathy and some balancing issues. My entire life had been plagued by ALD.

After first son died from CGD at a month old (only finding out diagnosis one day before he died), I was soon tested. I tried IVF two times with genetic testing —even though I had no fertility issues-but first time was miscarriage and second time it didn't take. We then looked into Foster to adoption, but that sadly didn't work out. 6 years later after death of first son we finally had another baby born (conceived naturally after prayer on what to do since no other options worked out), and he was healthy. We had one more boy a year later, he was positive for CGD. Luckily our middle son was the match so he underwent BMT at 17 months and is doing great today at 3.5 years old. I wish for more understanding and knowledgeable doctors and counselors about options, and not discouragement about having naturally and taking a chance as well...also knowing that learning to trust (God) is tough after loss.

ALD had affected my family since 1959 when my mother lost her younger brother. Both my older and younger brothers died from ALD. My maternal grandmother and mother died from ALD symptoms. My first pregnancy was a boy affected in utero with ALD. The pregnancy was terminated at five months. I did IVF with PGD in 1998 (only sex selection of embryos was available then). One of my twin daughters is a carrier the other is not. I found out that I am affected with symptom in 2019. I have severe burning neuropathy in my feet and some balancing issues. I have connected with support groups on Facebook which is helpful. Not knowing how things will progress is frightening. I know what might happen since I watched up close how ALD affected my grandmother and mother.

I think the most disheartening thing is that my paternal aunt had a diagnosis for her two sons, but never revealed it to our family. I never even knew they are blind. My father was incorrectly diagnosed. Had I known, we could have done IVF/PGD and spared our son and ourselves a tough life. I love my son to death and am so happy he's alive and ours, but I would not wish blindness on my worst enemy. Even though I could do IVF/PGD now (we are lucky enough to be able to afford it), I want to be able to devote all our time/resources to our blind son. So having another child isn't a good option for us. So many XL carriers in our group don't even know what reproductive options are available to them, and frankly there is shaming within our group if people choose IVF/PGD, adoption, etc.

I found out that I was a carrier 4 months pregnant and I was carrying a boy. It was the most traumatic experience of my life. I had to have amniotic testing to see if my son was affected. My doctor at the time was pushing for a medical abortion and I was an emotional mess. I would cry for weeks until I received the results of whether or not he had it. He was not affected, but due to all the stress during my pregnancy he did have issues at birth. I chose to abort - thank goodness, but I was upset that was what my doctor pushed for due to the horrible life my son would've have led if he had ALD. Also, my sister has two boys under 5 and she suffered immensely when I told her that she should get tested and her boys too. My mother and sister tested negative and I was told I mutated the X gene on my own. I feel extremely alone.

I have 4 kids, 3 girls & a boy at the end. We did not find out about ALD until the newborn screening when my son was born this past January. Had I known about my carrier status, we would have had kids through IVF to avoid passing it on. We still don't know if our daughters are carriers because they are minors.

I didn't know about alternative birth options until I was pregnant. I thought my choice was 50/50 chance at safe baby or adoption.

Aim 4: Needs / Priorities – Determine the priority of needs among X-linked carriers.

Women need more testing at different times in their lives birth pre-teen, childbearing years, pregnancies, and post menopause. More studies and standardized care for all women birth to death.

This issue became so important to me that I formed the CGD Association of America to advocate for patients AND carriers. :)

The question about what age should females be informed is such a challenging one, complicated by potential for genetic discrimination. What age will women be screened? If you test at birth, what does that mean for insurance coverage, life insurance for your child.

We are new to the X-Linked ALD diagnosis. I will help to collaborate in any way that I can to shed more light on this disease.

(Specific to family planning)

If I would have known I was a carrier prior to having my daughter I would not have had my daughter at all. She has been such a blessing on my life and my outlook on life. The question of having more children is still in the air but as it stands now I do not plan to have more and it makes me sad. It saddens me to think that I would have to undergo to prevent passing this syndrome to another child as I think about the joy and blessing my daughter brings me. It is a tough question. Finding out later in life was a blessing because of my daughter but it still poses lingering questions I am trying to navigate.

I don't know if I would have chosen not to have children, but I definitely would have considered it. The answer choice in this survey was limiting.

As an x-linked carrier with a daughter who was conceived naturally, my biggest concern at this point is navigating when to get her screened and how to talk to her about it. I would also have a second child if this were not an issue, but the cost and emotional burden are huge barriers.

Having learned at a young age, I used birth control until I had a medically necessary (unrelated) hysterectomy at 25. I chose (and was blessed with the choice) to not carry natural children that would inherit the disease. Now that I have symptoms and don't know what the future holds, I'm still glad I had the choice.

My 3 sons were diagnosed after my 5th child was born...I would have definitely benefited from being able to make an educated decision about how I would have my children.

I have spent my adult life worrying about my future and my children's future. That is a lot of stress! Because there are no predictable answers. I was shocked when I learned I was more than a carrier. And though I knew the risks of passing this onto my children I desperately wanted children. It is all such an emotional rollercoaster and the stress is of worry and concern definitely takes another toll on our physical and mental health!

I had genetic "counseling" before I had kids (because my sister has adrenal insufficiency) and was told I couldn't pass on something I didn't have. After my son was diagnosed with ALD, I realized that my sisters AI is from our shared ALD. We decided not to have any more children (already had 3) and my sister, who had just gotten married, decided to adopt.

My carrier status diagnosis has most greatly affected future family planning. I could have gone through IVF with PGD earlier and potentially not had the same issues, barriers and stressors that I had going through it after my son's birth.

Other: Responses that did not fall into an aim category

For me the biggest effect was the guilt of giving my son his condition.

I am 89 so it is a little late to help my family.

I have two children. First was conceived through IVF. I was genetically tested for "everything" and came up perfect. Then, my son was conceived naturally and it was quite a shock to find out he had a genetic disease. They just don't test for it for IVF unless they know they have to. So it was extra frustrating. In the end, I love my son but always wonder had my prenatal care been different, maybe his birth (and subsequent first months of life) wouldn't have been so traumatizing for both of us.

Met my bio-mother and 1/2sister Nov. 1999, after long search, son age almost 4 with issues that didn't make since mom and sister I tested myself for a carrier I was, tested both my children both my kids have it my son was a three-year-old at the time and has now passed in 2017.

Testing before giving birth for everybody.

It feels hopeless.

I wish a microarray would have been performed before I had children. I went for genetic testing but they didn't do a microarray.