

## Appendix B. Quotes From Structured Interviews and Focus Groups

### **Box 1: Context of Limited Empirical Evidence**

**[1a] Parent participant (10016):** *“The most difficult part, I guess, is the unknown....I think the most difficult piece of it was just the lack of information in one location. We had to go through so many avenues to get the information that I needed to feel better about the decision that we were making. I needed all the information, and we had to go everywhere.... That’s the hardest part. It’s so hard to make the decision when you don’t have all this data.”*

**[1b] Provider participant (20001):** *“I think just the uncertainty of what is going to give their child the better long-term outcome is really hard...The fact that I can't totally resolve that uncertainty”.*

**[1c] Provider participant (20026):** *“Lack of us knowing what we're doing [is most challenging] ...we need to get more data to know what we are doing. Are we really helping them or are we doing more harm? Do we need further stringent criteria to decide on this or is what we're doing okay? I think those are the questions that we need to answer...I think it's lack of data and knowing if we are doing the right thing for this child or if we are actually harming them more than we are helping.”*

## **Box 2: Weighing the Relative Risks and Benefits of Available Treatment Options**

**[2a] Parent participant (10001):** *"We wanted to be in the driver's seat...for his best interest and his life...it's the same thing as a risk/benefit. You're making a pro and con list, and it's an unknown number of hyperammonemic episodes versus unknown complications from liver transplant. I think it's a hard decision, especially in those that might not be extremely sick right now."*

**[2b] Provider participant (20011):** *"Most challenging for the families – I think...they're probably, in many cases, wrestling that risk/benefit ratio. They're saying, 'How much chance do I want to take with my baby?' When we tell them how sick their baby can get from hyperammonemia, and then they hear from the surgeon how tricky the surgery could be... I see that as being a tough balance to accomplish."*

**[2c] Provider participant (20001):** *"I think the risk-benefit is much easier for families to see in kids that get transplanted for other things...where the kid is literally getting sick before your eyes in the hospital...we can tell you rather definitively that the only way your child is going to survive is to get a liver transplant as soon as possible. I think those decisions are just easier to make. The risk-benefit is much easier to assess because you can see how sick the kid is and how much medical support they're requiring... it can be much harder [in UCD] because the child looks okay and you're going along life as you've been doing and they have limitations but you get used to it. It's a really different decision, I think."*

**[2d] Parent participant (10023):** *"It just seems like – because there's no standard practice in these cases, it's extremely difficult. It feels like we're on the frontier of this thing, and it's not clear what the right decision is...we feel like we're making a decision, and we don't really have all of the information...Maybe that's just because that information doesn't exist."*

### **Box 3: Phases of Childhood and Developmental Milestones**

**[3a] Parent participant (10021):** *"I was talking to the dietician about green beans, and she said, 'Well, once he's taking more than a few tablespoons at a time, I'm going to have to know how much he had so I can take some protein away from him out of the formula.' I really thought, 'Man, this is the easy part. Mixing formula every day and measuring, that's been easy compared to knowing specifically what's going in his mouth.'"*

**[3b] Provider participant (20011):** *"The cadence of care for these kids is they have catastrophic episodes. Then they have a little honeymoon. Then they're about roughly six months to a year old when they don't have much happen to them because you control everything that goes into them. Then you start feeding them. They get a little rockier. Then they're up and down, and up and down."*

**[3c] Provider participant (20006):** *"Having to deal with unpalatable medications, how to get their kids to take them, and I think dealing with compliance for a long-term, complex, medical condition is difficult, especially with – hard as toddlers, and then it gets a little bit easier, and then you have an adolescent who wants to have some control over their lives, and refuses to take their medicine, or says they do and don't, and things. I think those are a lot of things that our families struggle with."*

**[3d] Parent participant (10019):** *"She went to a preschool classroom two days a week, but if any of the kids were sick or if she was not feeling 100%, she was probably not there as much as half the time. She missed a lot because we just constantly had to monitor certain things."*

**[3e] Parent participant (10023):** *"The doctor made it pretty clear that she probably won't go to a normal school. Yeah, the diet poses serious challenges if she's going to be going to a school. We haven't figured that problem out yet."*

**[3f] Parent participant (10019):** *"If she would've missed one of her doses of medicine before her transplant, that was a guaranteed ticket to Hopkins. As she became older, and she didn't need mom and dad to shove medicine in her mouth anymore, and it became her job, for sure, I thought about that and worried about that, probably more as a teenager."*

**[3g] Parent participant (10014):** *"It's just a new chapter in our lives. In order for [my daughter] to – the possibility of her being able to maybe go to college and – I'd like for her to be able to go to college and maybe go away to college someday...just be able to think about things like that. I don't know. If we can't get it under control now, I don't know how we're going to be able to get it under control in the next couple of years."*

**[3h] Provider participant (20005):** *"Especially with the older children, are you getting older, and who's going to take care of this – who's going to manage the child who doesn't have a liver transplant after you're dead and gone or if you become incapacitated? If life goes on, you never know what's going to happen around the corner. With the younger patients, I usually don't take that approach, but as the patients get into their teenage years, it's a question of, well, who is going to manage this, a sibling, and are they willing to do it? That's something that really is important to think about."*

#### **Box 4: Tipping Point**

**[4a] Provider participant (20010):** *“Finally, push came to shove where it was the kids were coming in too frequently, or their ammonias were being too problematic, difficult to treat. Then we finally made the decision when that balance or the scale seemed to tip... Every child is different, and every child comes in with a different set of issues. Whether it’s the diet, whether it’s the medicine, whether it’s just the lack of activity or just feeling out of it all the time, whether it’s hyperammonemic crises, bringing them in frequently, these are all issues that come into the play of whether or not you go ahead and you finally make a transplant decision.”*

**[4b] Provider participant (20011):** *“Families take that information in different ways. I’ll have kids that I think have a little bit milder disorder, where we’ve talked about transplants because I usually do in the urea cycle defects. I at least let them know what the spectrum of options are...The family, well, when can we do the transplant? I say, your kids aren’t that sick. Then we have other ones where the kid’s coming in once a month, and they’ve had many [hyperammonemic episodes] ...and the families say, oh, I don’t know if I want a transplant.”*

**[4c] Provider participant (20012):** *“For some caregivers it’s right away. They want the transplant right away. They want this condition gone. This condition scares them way more than a transplant. There are some caregivers who, within a year, would say, “I want a transplant.” ... Some families just reach it right away and others have to sit for a while with it.”*

**[4d] Parent participant (10026):** *“It was his second crisis then at 10 months, I guess,...that tipped the scales.... After the second crisis, there was – we didn’t feel like it was a – it was a decision that was definitely transplant.”*

**[4e] Parent participant (10002):** *“Honestly, as caregivers we were not handling it well. We were handling it but to think of living years like that, with that kind of fear, was overwhelming.... I think for us it was the fear of her just having a completely severe decompensation to the point where she’d have a really severe brain injury and that her life could completely change in an instant... I think it’s one thing that if your baby’s born a certain way and that’s what it is and you deal with that situation. When you’re just constantly facing it but knowing that you’re not there but that everything could change for them at any time, to me it’s just a really different way to try to exist with just the fear of it.”*

### **Box 5: Disease Severity**

**[5a] Parent participant (10004):** *“He had almost a complete deletion in his chromosome. Anything could just set it off...They were like ‘It can go off anytime. It can cause another hyperammonemic episode... He could possibly die, or go into a coma, or have seizures...This is his best chance of survival.’ That’s what we did....it was really the only long-term option for him.”*

**[5b] Parent participant (10006):** *“[He] had 0% of the OTC enzyme. Honestly, we really weren’t given a choice. It was sort of a no-brainer like, okay, you live in fear for the rest of your life that when he gets sick his ammonia will go up and cause further brain injury. That’s what we chose really with the guidance of the metabolic team.”*

**[5c] Parent participant (10023):** *“I don’t really know. I feel like she’s probably always going to be a little bit unstable. We seem to be in and out of the hospital every three months, about. I don’t know. She has zero enzyme function, so it’s pretty black and white in her case.... I feel like things probably aren’t going to change very much, but who knows?... Do we do it now and protect her neurological development, but then risk her life, or do we continue with conservative management in the hope that maybe an alternative treatment’s going to develop?”*

**[5d] Provider participant (20006):** *“I think in the severe neonatal onsets; I think that’s less of a question at this point. That’s really the only way to save them....I think that in that case, there’s...less question about whether it’s the right thing to do...In the later onsets, where it’s a little bit less clear-cut, I think – we have extensive conversations.”*

## **Box 6: Disease Stability**

**[6a] Parent participant (10007):** *“He was in the hospital every week or so because his ammonia would shoot up, and we really had no control over it. No matter what diet, how we adjusted his diet or his medications, his ammonia would always just go up. It was necessary for him to get a transplant because we couldn’t really control his ammonia.”*

**[6b] Parent participant (10002):** *“In her case, we just couldn’t keep her stable. She was pretty stable for two months before she was hospitalized again, but she had a handful of decompensations within the first few months. We were already feeling pretty desperate in talking about transplant within the first three months of her life”.*

**[6d] Parent participant (10005):** *“Initially, we were not for transplant. I, of course, did all the Google stuff, which I know you probably shouldn’t do, but I just saw all the complications and the constant taking of medication. It just didn’t seem like something that we wanted to do. We thought, oh, we can keep him managed, but basically, it started getting to the point where [he] was beginning to have to be hospitalized every couple of months for illness.”*

**[6e] Parent participant (30002):** *“From everything that I’ve heard, it should be for us more of a last resort scenario. My daughter’s condition, for the most part, has been pretty well-controlled. She’s had some, a few, maybe three or four high ammonia episodes in the last ten years that required hospitalization, and those were mostly well-controlled. In my mind, if that is still feasible for us, why would we take on the risks that are associated with the liver transplant?”*

**[6f] Parent participant (10008):** *“Tons of reasons as to why we felt transplant was a better option, even though he was quite a stable kid so far, but everybody told me that might not be the case forever. That can change literally overnight, so that’s why we decided to go for the transplant.”*

**[6g] Parent participant (10031):** *“She is stable. She’s met all her developmental milestones. She is thriving. You look at her, and she is very typical...So when she went into the [transplant] doctor’s office, they’re looking at us like, okay, she’s fine right now...but what about when she has her next one and...what is that going to look like? That terrifies us.”*

## **Box 7: Burden on Familial Unit**

**[7a] Parent participant (10010):** *"I'm like, oh my God, she never would've been able to do this...It would've impacted our lives, as well...just your daily life and meal planning. Those little things that I sit and think about, when I get overwhelmed with anything going on in her life now, I'm like, what would it have been without [transplant]?" and then I'm like, okay, I'll take it."*

**[7b] Parent participant (10011):** *"Before it was every night I never left things undone because it was always, oh, is tonight a night we're going to have to race off to the hospital?...Like I said, [transplant] changed our lives in a lot of ways."*

**[7c] Parent participant (10017):** *"It really impedes your life, your family, and I wouldn't want that for any new family. If we could protect them and they don't ever have to go through it, and if transplant is safe, with it being as safe as it is, then that's always an option. That's the best option...the lack of sleep and constant worry, completely sleep deprived because you check to make sure they're fine all night long. The stress of what if something happens, that takes many years off your life."*

**[7e] Parent participant (10013):** *"That has definitely been a challenge, just to have a healthy amount of and realistic amount of worry, not to let yourself fall into that pattern of panicking...this condition is not for the faint of heart. Managing it, I'm not going to say it's easy by any means, but it is doable...Despite all of our ups and downs and things we have to go through when we think she's sick, I'd still rather deal with that than have to deal with X% dying and all the issues that come with having a major organ transplant... I just don't see a reason. The path unknown is really frightening to me, and there's no reason for us to go down that path unless we need to."*

**[7f] Parent participant (10027):** *"Right now, he is living a 100% functional, wonderful life. Getting a liver transplant would just be replacing his urea cycle disorder with another condition. He would be on...immunosuppressant drugs for his whole life. I feel the way I manage his urea cycle disorder, I would have time if something were to happen. If he were to get the flu, or some horrendous illness that would spiral his urea cycle disorder into a horrible ammonia attack, we'd have time to deal with that....If he gets the flu, I can usually manage it from home...I feel like if it was a liver rejection, and say there wasn't another liver available, I wouldn't have all these options. I wouldn't have the options to save him the way I could now with a urea cycle disorder. That's why I've chosen not to transplant him."*



## **Box 8: Burden on Child**

**[8a] Parent participant (10012):** *"I remember she would wake up every morning, and she'd be just moaning...I don't know if it was pain or if it was...just foggy ammonia brain....She was just never normal.... It was just very – I don't know. It was very sad...It was day-to-day. It was hell. She would be stuck to a pump for an hour, and then we were still at that time trying to feed her orally. We'd sit her down at the table, and she'd sit for hours just trying to get a little bit of food in, and then by that time, it was time for another feeding. I mean, she had no life. She couldn't play. I mean, she was miserable...her thoughts were disorganized and cloudy. She wasn't a normal kid. It was heartbreaking."*

**[8b] Parent participant (10018):** *"That was one of the things in school. He learned how to count money, and that was a huge thing because he worked and worked at it. Then he had a high ammonia level...He remembered that he knew how to count money, but he couldn't count it anymore. We thought, oh, that quality of life's horrible. That was another one of the things that – especially he had to work so hard to learn it more than just a normal kid, and then to lose that functionality was devastating for him. That played into [the decision to transplant] too."*

**[8c] Parent participant (10019):** *"We didn't let her do a whole lot outside of our house, in terms of being normal, regular kids that can go play, and go swim, and go to school. We were too worried constantly about what she was going to get into, or was she going to burn too many calories, or was she going to wear herself out. We just kept her in a bubble. It was very stressful."*

**[8d] Parent participant (10024):** *"He's very active. He's very involved in sports...he plays football. He plays basketball. He plays lots of sports. [The doctor] adjusted his metabolic formula. She adjusted some things...He, obviously, is gaining weight. He's growing. His height, he's getting taller. He's doing so much better."*

**[8e] Parent participant (10013):** *"Of course, there's worry, but she doesn't live in a bubble and she never will. I want her to be out and about and to be part of normal life. It's just she's going to have to take more precautions than other people."*

### **Box 9: Peer-to-Peer Interaction**

**[9a] Parent participant (10008):** *"I probably wrote back and forth with probably about six, or seven, or eight different moms for a couple months. Just hearing their experiences, asking if they feel that dealing with transplant life is easier than a UCD life, and all of them told me that they absolutely thought the transplant parent life was better than UCD life. A lot of their opinions really helped make my decision."*

**[9b] Parent participant (10017):** *"Recently, a girl that is 14 that's had a really hard time for the past 5 years, she was transplanted. That's someone that is close to [my daughter's] age, someone that [my daughter] has known... Seeing that and hearing how well she's doing, I think that's going to make her process a little easier."*

**[9c] Parent participant (10014):** *"There is a girl... We met her at a urea cycle disorder conference... Wonderful young girl and she got a liver transplant, and she is doing wonderful... It's neat because [my daughter] is like you're just like me. You're just like me."*

**[9d] Parent participant (10015):** *"I had talked to one parent who had lost her child with ASA when she was 18 years old, and other caregivers whose kids' livers were doing really poorly in their teens, and I thought, I should just preempt this now. I'm not going to do this struggle of trying to get him to have nutrition, watch his brain deteriorate when it's not preventing the hyperammonemias, and just to get him to a teenager where he's going to die anyway. That made me request the transplant."*

**[9e] Parent participant (10011):** *"A good friend of mine lived nearby in. Their daughter was transplanted. She died. It was a bad – things just went poorly the whole way through... I don't think she ever even came home from the hospital after being transplanted. That left a bad taste in my mouth, and between that and the fact that our doctor was very adamantly opposed to doing a transplant, for a long time we didn't even really give it much thought."*

**[9f] Parent participant (10013):** *"We've lost touch with them because now they're on a different track; they're being followed... post-liver transplant. From what I understand, it hasn't been an easy road for them at all. She's been stable... but it hasn't been easy at all. It, in my opinion, reaffirms why we never went down that path. What I've heard from other people going to various conferences is that it's trading one set of issues for another set of issues. If we don't have to find out what those other set of issues are, why would we? That's our thought process."*

**[9g] Parent participant (10027):** *"We felt like we were all alone, and then all of a sudden, these people just pop up, and here they are. They have this son who is... I think he was five at that point. It was just incredible... This mom was like, 'Look, this could be [your son]. This could be [your son] in five years.' It was a completely different outlook on what we were thinking... They're handing our infant to us, and we're thinking that he's going to die. Then all of a sudden, we have this other family that says, 'No. Look. Look. We have this son. It hasn't been easy but look at him. He is beautiful and healthy.'"*

## **Box 10: Considerations for Child's Independence**

**[10a] Parent participant (10018):** *"At one of the meetings at the Urea Cycle Foundation...they talked about...He was living on his own, and he died because his caregivers couldn't get hold of him. When they found him, he had had a high ammonia episode, and nobody was there...That made it an easy decision. We'd never let him live alone...When he'd get sick spending the night at his cousins, we were like heck, we don't want to let him spend the night anywhere. We don't want to take the chance...What kind of a life can he have if someone has to be watching him 24-hours a day?...Some of those episodes came on so fast that even if he was a normal adult, he might not have been even able to call 911 in time to manage it for himself."*

**[10b] Parent participant (10017):** *"Because [she] has done so well in school and has done so well socially, going to college...that is a very good possibility, where we never really thought that was a possibility. For her independence, a transplant is necessary...It is something that with OTC and when her ammonia level starts to rise, she can't make decisions on how to help herself. There always has to be someone there to help her identify and help her make changes to her diet and to her medication before it gets too bad. Living on her own and going away to college was not going to be an option."*

**[10c] Parent participant (10013):** *"It's a constant struggle as I'm trying to prepare her to be a young adult, understanding that in order for her to live her life, she has to be her own caregiver. That's another huge hurdle of what we're going through right now, saying, 'Okay, this was your responsibility. We're not going to be here all the time to monitor what you eat, whether you're taking your medicines,' and right now that's the biggest challenge we're having as a family...Like I tell her, if she wants to go off to college and wants to have a job, I'm not going to be there to ask her what she's eaten or whether she's done her medicine; it's all going to be on her. It's definitely a process. She's not fully aware yet, but there are signs that she's finally getting it."*

**[10d] Parent participant (10025):** *"Even right now, she's 9 and in the third grade. We're trying to transition into getting her to read food labels. Getting her to understand what everything – right now I mix up her medications, and I measure everything. We already talked about, okay, how old does she need to be before she starts getting old enough to do that? Yeah, that's our goal. We understand some day she's going to leave the nest. She's going to need to know how to do all of this. At one point do we start teaching her?"*

### **Box 11: Access to Quality Metabolic Care**

**[11a] Parent participant (10008):** *“Yeah, the quality of care. Part of my decision [to transplant] too was UCD being so rare. What I was told is I can’t be on vacation and be sure to find somebody that’s even going to know what I’m talking about. Even our local hospital didn’t even – they had no idea what a UCD was. They had no idea how to care for him. I just felt it was really dangerous for him to live with that disorder in the future, for his life.... I didn’t feel like I was getting much help with the nutrition aspect, and I was worried about that for the future because it’s such a huge part of keeping him healthy... Then a couple of times...he had an emergency. He had been vomiting all day, and we took him to the ER. Of course, the ER was terrible. They don’t know anything about urea cycles.”*

**[11b] Parent participant (10026):** *“All these little things were adding up for us. Okay, he didn’t have a crisis for eight months, but they’re not able to quickly handle it. This is a hospital that actually knows about it. I had talked to plenty of caregivers whose child had brain damage because they were in a place...where the hospital didn’t know about it. Ours knew, and they still took days to get this going and get him stabilized....we just looked at each other and said, if we weren’t here watching like hawks all the time, would he survive?...When we went in there, my faith was that these people were going to save his life, and suddenly, I couldn’t count on them to do it right. You know?... The head of transplant came in, and said again, ‘I think you need to talk to us again.’ We said, yes, we wanted to get him – we changed our minds. We want a transplant.”*

**[11c] Parent participant (10012):** *“We’re here...with very limited access to a decent metabolic geneticist. I’ve been told there just aren’t that many, I guess. There certainly aren’t any in this state, and so it’s just access to good care, basically...It seems that there are only a handful of specialists throughout the country, and if you’re not in that location, you’re really subject to pretty subpar care.... Not being able to rely on your healthcare provider. I mean, I think the question had to do with local – not having local access to good physicians. We never felt like they had our backs here. We could never rely on them. We would put a call in and not – we wouldn’t get a call back for a week. When you’re trying to manage day-to-day, it’s like, oh, we got these labs back. What do we do now? You can’t wait a week. I mean, it was horrible, so that was a huge stress for me knowing that we were basically on our own.”*

**[11d] Provider participant (20021):** *“If you have a medically unstable child who lives a long way from a facility with any special expertise with urea cycle disorders, he could get into trouble quite easily and not have medication at hand that they need. That obviously does change the balance of how you would recommend liver transplant... I have a [adolescent] patient who – she was really well her whole life, but then...had one or two hyperammonemic episodes, not even that severe, quite moderate. Because of her geographic location, I recommended transplant because her ammonia control baseline wasn’t that good. I was worried about compliance, and I was worried about her geographic location, so we listed her, and she was transplanted last year.”*

**[11e] Parent participant (10028):** *“I’m confident that if she does get sick that we’re in the right place. I trust the team here very much... Here, anytime there’s been a question of high ammonia, they’re like come in. Let’s do labs. We wait in the hospital until we know what the number is...The reason [liver transplant is] not forefront in my mind is because we are with [this] department, and we’re with [this] doctor. I’m very confident in our team on our day-to-day management and how we do everything...If it’s decided that we can’t stay here... I pretty much know transplant would happen in one of two facilities, and then we’d go from there.”*

## **Box 12: Metabolic Physician Approach to Treatment and Guidance**

**[12a] Parent participant (10027):** *“I had such an incredible team that I really didn’t have to navigate it alone. They were really there for me...The doctors have been incredible...I never really had to navigate those things alone medically.”*

**[12b] Provider participant (20001):** *“I think [the family’s] view of transplant is impacted significantly by the impression they’re getting from both the metabolic genetic team, who usually know them really well and is really involved with them, and the transplant team that they see. From what I’ve heard from other doctors and from families, they may get a very different impression of what transplant involves and what the long-term outcomes are depending on who they talk to.”*

**[12c] Provider participant (20001):** *“It seems like the discussions I’ve had with geneticists is that people have very different approaches at different institutions.... Some people have very clear ideas about who they refer for transplant, and some people don’t. I don’t think we know which one is the right approach...I was definitely surprised about that when I started talking more to metabolic geneticists at other centers or that had recently come from another center to ours.... I think it has a lot to do with, especially if you only have a few cases and then you have even fewer cases who decide to go through transplant, what happens to them afterwards. If you see a bad outcome or two that can totally change your impression for the next 20 years versus if you see some who do really, really great, then that may also change your referral pattern.”*

**[12d] Parent participant (10011):** *“He was very, very anti transplant, very anti transplant, just really had nothing positive to say about it, and he remained that way. I will say that’s part of the reason [my son] was so much older; why we didn’t give it more consideration...There were a few periods where he was really sick for a really long time and almost died a couple times, and still, this doctor held fast. He did not think transplant was the way to go...When I’d bring it up to the doctor, he still was not in favor of it, so we just didn’t really push.... I still was not positive it was the right – at that point, I still was a little unsure. I mean, having a doctor for 20 years that is the top of the field saying don’t do it. Don’t do it. It’s like, oh, man, are we asking for trouble doing this?”*

**[12e] Parent participant (10019):** *“I would say, for our family, one of the biggest challenges was that we didn’t have support from our genetic team... They weren’t encouraging a transplant. [The hospital] believes that you’re much better to manage the disorder. Because we trusted these people because they saved her life and because they kept her alive, we had our full trust in them with how to handle her. Then when we decided to look into transplant, and it wasn’t even something that we could bounce ideas off of them; it was something we just didn’t talk about. I would say that was, for us, one of the bigger challenges.”*

**[12f] Parent participant (10012):** *“We mostly spoke with the geneticist...and if you’re familiar with him at all, he is of the mindset that if you’re born with OTC, basically, you need a transplant. With that mindset, it just – it was like this is happening. This is the best solution. Oh, yeah. By the way, there are risks, and here is what they are. It wasn’t even like a risk benefit analysis so much. It was just be prepared. These are the things that could happen, full well knowing that this is going to be a far better choice for your daughter at this stage. That was already the foregone conclusion, I think, when we arrived.”*

**[12g] Parent participant (10031):** *“We did pursue transplant. [Our doctor] has just been open to what we as caregivers feel comfortable doing. He thought it was important for us to explore and see what would be beneficial for [our son].”*

**[12h] Parent participant (10023):** *“It just seems like – because there’s no standard practice in these cases, it’s extremely difficult. It feels like we’re on the frontier of this thing, and it’s not clear what the right decision is, and nobody really wants to say one way or the other.”*

**[12i] Parent participant (10008):** *“I mean, if I could change it, I really wanted to have more guidance from [my son’s] metabolic doctor, but he never really gave much of an opinion.”*

**[12j] Provider participant (20006):** *“What we often tell the family is that there’s not a right answer here. It’s not wrong to choose one or the other. It’s what’s right for them as a family together. That, I think, is difficult for families because in something so major, I think what they really want to hear often is, ‘This is what you should do. This is what you need to do for your child.’ Making that decision and putting it on a family is really difficult. I always feel that when we have these discussions that I wish I could just tell them what to do. I think that would take a lot of the burden off the family.”*

### **Box 13: Cost and Coverage of UCD**

**[13a] Parent participant (10005):** *"In the very beginning I had to do a lot of navigating with [my child's] medication, the sodium phenylbutyrate...They did not want to cover it...I spent many hours on the phone for about a month after [he] was born, having to get him what he needed...The actual cost and coverage with [his] transplant, we have not had to worry about that at all. That was covered. We never got any issues and trouble for it."*

**[13b] Parent participant (10030):** *"The transplant coverage has been beautiful...After surgery, we accidentally left [medication] in our refrigerator, and we went [on vacation]...Even though we were out of state, the insurance company was more than willing to pay for a small amount of medicine to be made right there...at 10 o'clock at night. Otherwise, we were looking at turning around and coming right home. That's what we would've had to do, and we were prepared to do that...The insurance was like, no, no, we'll pay for five days' worth."*

**[13c] Parent participant (10017):** *"It's too hard...insurance, and the cost, and the struggle between insurance, and where you work, and getting covered, and it's not just one medication, it's multiple, it's a full-time job just to get medication. The amount of hours that I have spent just to get medication sent to our front door, we've driven all over the place and had things flown in overnight all the time. It's too much...First is what is covered under your insurance. Part of the treatment is medication, but the other part of the treatment is the nutrition. The nutrition many times is not considered medically necessary but is medically necessary...Then you're constantly battling with your insurance company. It's hard enough emotionally to deal with the condition, but then to have to be bullied by insurance companies. So many, my family included, but so many families have given up so much of their time and money. The amount of money that we spent the first five years that [she] was diagnosed, we were living in poverty, but our income was well above poverty...we couldn't comprehend how it could cost this much money out of our pocket to be able to keep her alive....Then your insurance company – every time you get a call, you think this is when they're going to cancel us; this is when they're going to say they're not going to pay for this anymore."*

**[13d] Provider participant (20023):** *"I've had with families that surprises me they think about this early is cost of care. I've had families who really want to know how many outpatient visits are they going to have per year. How many expected inpatient visits are they going to have per year? What are the costs of the medications? Really very financial detail... we cover such a large geographic area, so it's not uncommon for our patients to be 12 or 14 hours away each way. They're really thinking about time away from work, spending the night, and coming to see us. I've been surprised how many patients have made medical treatment decisions based on those kinds of cost."*