

Appendix C. Caretaker- and Provider-Informed Dissemination Strategy for New Evidence on Treatment Choice in UCDs

A Caretaker and Provider-Informed Dissemination Strategy for New Evidence on Treatment Choice in Urea Cycle Disorders

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PURPOSE

- To propose a targeted, comprehensive, and feasible approach for the dissemination of (1) new evidence comparing outcomes of medical management and liver transplant as a treatment for Urea Cycle Disorders (UCD) and, (2) the treatment decision making experience of families who have navigated or who are currently navigating this treatment choice, which is patient-and provider-informed.
- To promote greater consideration of UCD patient needs and priorities in the future development of research products and dissemination materials.
- To cultivate discussion among researchers, practitioners, and patient groups on present day challenges to information sharing within the UCD community and viable approaches to a long-term, sustained improvement in the dissemination of current and continuously developing knowledge in the field.

METHODS

Data Collection

Qualitative data was collected directly from caretakers of children affected by UCD and their clinical providers through a total of eight, semi-structured focus groups (two live caretakers and two web-based caretaker focus groups; and one live provider and three web-based provider focus groups). Focus groups were conducted in sessions lasting approximately 90 minutes. Focus groups were recorded and transcribed verbatim for use in analysis.

Focus group guides were developed by integrating findings from a limited relevant evidence base as well as initial discussions with key informants from the National Urea Cycle Disorders Foundation (NUCDF) and patients and providers previously interviewed for Aim 2 of the study. Draft guides were reviewed by key informants, including families with children affected by UCD and metabolic genetic physicians specializing in UCD. They were revised and refined based on feedback from this group before being utilized in the field.

Sampling

The target population for this study included caretakers whose children were born in the US in 1995 and thereafter and diagnosed with one of the four UCD (ALD, ASD, CPS1, and OTC) for which liver transplantation is a consideration. Stratified purposeful sampling methods were used to recruit caretakers by the NUCDF from the patient community.

Recruitment focused on identifying participants who varied in terms of (1) disease severity (i.e., neonatal vs. late onset), and (2) transplant status (i.e., medical management vs. transplant).

Stratified purposeful sampling was also used to recruit a national cross-section of UCD providers for participation in focus groups. Providers were recruited via the Urea Cycle Disorders Consortium (UCDC) and the NUCDF to reflect variation in location and type of provider, including metabolic disease physicians, gastroenterologists, hepatologists, genetics counselors, advanced practice nurses/nurse practitioners, and dietitians.

Data Analysis

Initial data abstraction was conducted through the line-by-line open coding of two focus group transcripts. This approach allowed key issues regarding dissemination of evidence and information sharing to emerge directly from the collected data and ensured that important aspects of this phenomenon were not precluded through the use of a more selective coding scheme. Open coding was utilized to generate a preliminary set of codes, which was continuously refined until a final structure of codes and sub-codes emerged. This coding structure was then applied systematically across all focus group transcripts. Thematic content analysis was utilized to identify key patterns within the data and to categorize collected information into recurrent or common themes, which are described in the *Background/Landscape* and *Objectives* sections of this document.

All focus group data were managed and analyzed using QSR International NVivo 11 software.

Sample Characteristics

A total of 31 caretakers participated in four focus groups. Two of these focus groups had dissemination and use-of-evidence as the only topics of discussion. The NUCDF staff organized and observed the two in-person focus groups, assembled the two web-based focus groups, provided the web platform for holding the focus groups, and facilitated the process to ensure a smooth experience for all who were engaged in the discussion. Of 24 recruited providers, 19 clinicians participated in the focus groups, including 11 in the in-person focus group. All four provider focus groups were dedicated exclusively to dissemination and use of evidence.

The majority of caretaker and provider participants were female. Most caretaker and provider participants who filled out a demographics form indicated that they were between the ages of 30 and 39. The majority of children in the sample had neonatal onset of their UCD and received a liver transplant, with most undergoing the surgery before age five. The vast majority of focus group participants – caretakers and providers both – self-identified as white and non-Hispanic/non-Latino. All caretakers who filled out a demographics form reported having earned a bachelor's degree. Providers who filled out a

demographics form represented a mix of physicians (46%), registered nurses (27%), dieticians (18%), and nurse practitioners (9%). The most frequent specialty was genetics/metabolism (46%), followed by pediatrics (36%), hepatology/gastroenterology (18%), and family practice (9%). All providers were hospital-based and the vast majority worked for small (2-10 physicians) or medium (11-50 physicians) practices. The majority had been providing counseling and/or treatment for six years or less. A third reported seeing an average of 6-10 UCD patients per year and only one reported seeing over 50 patients on average per year. All reported encountering language barriers in their practice. The language most frequently mentioned was Spanish, followed by Arabic, Urdu, and Amharic.

Development of Dissemination Strategy Document

Developing a caretaker and provider-informed dissemination strategy followed a three-step process. First, the research team used the information collected and analyzed as described above to produce an outline of a dissemination strategy document, which was reviewed and refined by the NUCDF. Second, the research team and the NUCDF collaborated on drafting, refining, and finalizing the strategic document, sharing editorial control over the project. Third, the draft document was shared with the entire PCORI UCD team for review and final input before being submitted to PCORI as a deliverable for Aim 3 of the project.

BACKGROUND/LANDSCAPE: TODAY'S DISSEMINATION CHALLENGES AND CURRENT PATIENT-LED INITIATIVES

Our sample of caretakers and providers described a variety of present-day challenges and barriers to obtaining reliable information and evidence on treatment alternatives for UCD. . This section summarizes these challenges both from the patient and the family's perspective as well as from the providers' perspective. It also offers an illustrative sample of activities undertaken by the NUCDF, the internationally-recognized UCD patient advocacy organization, to address some of these challenges.

The Patient and Family

Caretakers identified the Internet as a key resource for information on treatment options. They discussed frequenting social media platforms, such as Facebook and Twitter, as well as the websites of individual institutions and the NUCDF for existing and developing information on medical management and liver transplant as treatments for UCD.

Caretakers described feeling overwhelmed by the (sometimes conflicting) information found on the Internet and found it difficult to assess whether internet information was valid, credible, or current. This was especially true for information accessed through Facebook peer groups where the content and quality of information are not vetted or controlled. Despite these challenges, caretakers still seemed to place high value on social media and other internet-based resources as a hub for information sharing and continue to

"As far as being overwhelmed with Facebook groups and social media because it truly can be overwhelming, and everybody has different ideas, opinions, facts...There's that fine line that if you get too immersed, you can almost drown, and you don't know what to believe and what not, but then I also found that if I stayed away completely, then I felt so alone..."

– Caretaker Focus Group Participant

utilize these websites to stay informed about new developments in the field. The NUCDF has worked to address these concerns. It is currently re-implementing and disseminating a tool for evaluating the quality and credibility of health information resources, including websites, handouts, booklets, social networking sites and other publications. The NUCDF also launched a moderated Facebook group (*Liver Transplant Support Community*) for families and patients that serves (1) as networking/support, (2) as vetted resource/information dissemination, (3) as a means to identify unmet needs and, (4) as a "listening" portal for feedback from families.

Currently under development is a NUCDF information hub website platform with areas for families, patients, and providers. Content will be reviewed by a medical advisory committee that includes UCD and liver transplant specialists.

Caretakers also cited their metabolic physician and clinical team as key and trusted resources for information about UCD treatment. Many caretakers expressed a preference towards physician-vetted information that is shared with them by their child's treating physician. However, many caretakers also cited concerns that the content and quality of information were not standardized across the field and varied significantly by provider, institution, and location. This information similarly varied based on the physician's approach to, and guidance around, liver transplant as a treatment for UCD. The NUCDF and the UCDC are currently updating and developing practice guidelines and resources. Clinical experts serve on working groups, including one focused on clinical practice resources for liver transplant. Families were able to provide input via surveys and a "*Developing Clinical Practice Resources-Patient & Caregiver Perspectives*" focus group conducted at the NUCDF Annual Family Conference.

"I've talked with people at a fair number of centers, and I'm always struck by how variable the sort of practices are. I think there are certain patients...that almost always get referred for transplant and other patients maybe that don't always, but I think it's quite different amongst centers, and...some folks send everybody to get education and evaluation for it. Other folks wait until they think it's really indicated for that patient, so it would be nice to have more formal guidelines about when an evaluation is indicated..."

– Provider Focus Group Participant

"You get such differing opinions from people on your own teams...you talk to different people around the country, you listen to [conference] talks, you get such different perspectives."

– Caretaker Focus Group Participant

When physicians expressed inherent opposition to transplant or failed to discuss transplant as a treatment alternative, caretakers often described feeling under-informed and/or compelled to seek information on transplant independently - suggesting the need for additional guidance and standardization around when and how information on liver transplant is presented to families affected by UCD.

Caretakers, who lived farther from either expert metabolic care or a trusted metabolic physician, seemed more likely to seek information through resources outside the doctor's office, generally via social media and website platforms. For these families, non-physician-based resources are utilized as an essential source for treatment information.

Caretakers described the NUCDF as a crucial resource for information and guidance on available treatments. Many cited their direct e-mail and phone communications with the NUCDF's Executive Director as a main source of advice and support. These communications were often motivators for seeking additional physician consultation and exploring other treatments, including transplant, which may not have been discussed with their primary

physician. Many described the NUCDF as a “life-saving” resource and hoped to see the organization continue to transmit and share its wealth of knowledge so that all UCD families, present and future, may benefit from the expertise and experience.

Integration of information between metabolism and transplant teams was another challenge cited by caretakers and providers alike. While metabolic physicians discuss the risks and benefits of continued medical management with caretakers, and may refer families to transplant consults for additional information on this treatment alternative, they rely on transplant teams to elaborate on the risks and benefits of the procedure and the short- and long-term clinical implications of that choice. What is often missing for caretakers of children with UCD is an integration of these two perspectives into one discussion about the relative risks and benefits of both treatments. The reality is that neither metabolic nor transplant teams are trained or possess the clinical knowledge to guide caretakers in this exercise alone which means that the caretakers of children with UCD must often integrate the information shared by both medical teams and come to a treatment choice on their own.

“There needs to be maybe a transplant representative...There seems to be a disconnect between...the metabolic group and the liver team...There needs to be some work to come together to serve the patient.”

– Caretaker Focus Group Participant

The Provider

Providers from metabolic, genetic, and hepatology specialties who participated in study focus groups noted a problematic lack of cross-education between the fields. Members of various liver transplant teams were eager to learn about new clinical findings that may better support treatment decision-making in UCD but were uncertain if their specialty would be targeted with this information. Physicians from both metabolic and transplant

“I know what to tell families about what they could expect after transplant, but...I can’t really help them compare, what are the risks of staying on non-transplant therapy. I think I would benefit from knowing a little bit more...just to hear from a metabolic person...what they think are the risks of maintaining people on diet. What are the challenges they face...I don’t really hear that side of the story, so I think it would help me understand...why I get referrals from some patients while others are never here.”

– Hepatology Provider Focus Group Participant

“I definitely cannot give the transplant information that they’re going to really need to make an informed decision, so I don’t think it’s fair for them to get it from me...I feel as though I don’t have enough information about the changing landscape of transplant.”

– Metabolic Physician Focus Group Participant

specialties also expressed some hesitancy in taking ownership of treatment recommendations for UCD patients. Neither group felt equipped with enough expertise on both treatment types (i.e., medical management and liver transplant) to appropriately weigh their relative risks and benefits.

Focus group participants cited concerns about the ability to reach providers who practice outside of expert metabolic care centers with new evidence and developments from the field. Many patients and families seek care from clinicians who practice outside the UCDC network, including other specialists, general pediatricians, and hospitalists. Anecdotally, these practitioners are less likely to interface with experts in the field, read journals that publish findings from UCD-related studies, or attend conference presentations on developments in UCD care and treatment. Without access to developing evidence and information, physicians outside expert metabolic centers may be ill-equipped to provide UCD patients and families with appropriate clinical guidance. The NUCDF is developing an annual meeting of liver transplant and UCD specialists to convene for the purpose of sharing information, research and treatment updates, and developing patient and Continuing Medical Education (CME) resources, which will be housed on the NUCDF's website with other provider education videos.

“Unfortunately, despite our best efforts and over decades, it’s very hard to get people to become familiar with conditions that they don’t see. Unfortunately, it can take a very significant event to make people understand what we know and understand about these conditions.”

— Provider Focus Group Participant

Even among providers within the UCDC network, focus group participants noted a lack of standardization in terms of how, what, and when information on treatment options is shared with UCD patients and families. Some providers present liver transplant as an available treatment alternative to all UCD patients; others limit conversations about liver transplant to only the most severe in their patient pool. Some providers aim to discuss transplant as an available option shortly after diagnosis or early in their relationship with the patient and family; while others believe in a more step-wise approach where transplant is introduced slowly only after patients and families have had an opportunity to cope with the initial diagnosis and management of the disease. These variations suggest that patients and families may not receive the same type and level of communication from their providers about new information on the relative risks and benefits of medical management versus liver transplant.

“I’ve trained in [several] different places, and I’ve worked in [many], and I’m not working where I trained, so I’ve seen so many different ways to manage – how to peel an apple. I can tell you five different ways to peel an apple, so I know that there’s going to be variation”.

— Provider Focus Group Participant

OBJECTIVES

The following describes potential short, medium, and long-term dissemination strategies for new evidence produced on the comparative outcomes of the treatment for UCD and the patient and family experience in navigating these treatment options. These strategies were developed from the focus group information collected directly from caretakers and providers and designed to address the current dissemination challenges outlined above. The NUCDF actively engaged in the overall strategic initiative around dissemination, collaborating closely with research partners during all stages of development and publication.

Short-term Strategies Targeting Patients and Families

Patient Conferences and Webinars

Conference presentations targeting UCD patients and families were highlighted as an appropriate and effective mechanism for delivering new information and evidence on treatment alternatives. The NUCDF annual conference was cited by patients and providers alike and is a natural venue for patient-tailored presentations on new study findings. Not all families are able to attend this in-person conference. To ensure that all families have access to these presentations, researchers should consider developing webinars that can be accessed live and as a recorded session through the NUCDF website.

Under development: The NUCDF is preparing webinars, presentations, and educational modules; some in collaboration with the UCDC.

Written Materials

Caretakers also sought and valued written materials on treatment alternatives that they could easily reference and return to at any time. Published peer-reviewed articles from traditional academic journals are both challenging to access and difficult to interpret. Thus, a layman summary of new study findings written specifically for consumption by patients and caretakers (similar perhaps to the layman’s summaries titled “Research Briefs” published by the NUCDF) would be a useful dissemination tool for families affected by UCD.

Caretakers did express a desire to read both the original published work as well as a summary of its key points and implications. Ideally, researchers would make both peer-reviewed and summarized materials available to the patient community.

“I like to get things in writing, whether it’s printed or online so that I can go back to it. Particularly, when you have a child that’s first diagnosed, it seems very overwhelming, and you don’t necessarily remember all the details that somebody tells you...”

– Caretaker Focus Group Participant

Under development: The NUCDF “Research Briefs” will be used to disseminate information from the UCDC studies and will be made widely available via the NUCDF and the UCDC’s websites, newsletters, and e-communications.

A set of “questions to ask your provider about medical management and liver transplant” was also suggested as a patient-level dissemination tool. Although not mentioned by name, it is worth noting that in 2017, the NUCDF developed a similar tool, which primarily

“At the very beginning...we didn’t know what to ask. It was just a slap upside the face...So some frequently asked questions...along with some places they can go get it...We’re not exactly sitting in a huge metropolis, so we don’t have access to those services that some people do. That makes a big difference. ”

-Caretaker Focus Group Participant

focused on liver transplant, titled “Transplant FAQs.” This list of questions was reviewed with families and disseminated to the Liver Transplant Support Community Facebook group, to study participants, and to families who contacted the NUCDF for information and support about liver transplant.

While many caretakers have a preference towards information relayed to them by their physician, many also do not feel equipped to navigate these important conversations and need

additional guidance on the key questions their provider should be answering and the types of information they should seek from their care team. This list of guiding questions, which would include, among other things, prompts around the development of new findings in the field, would empower patients and caretakers to take ownership of their own medical care, while also recognizing the key role that physicians play in disseminating information to the patient community and ultimately, in guiding treatment choice.

E-mail and Listservs

E-mail and listservs were cited as a common mechanism for distributing UCD-related information and an effective way to reach patients and families with newly developed webinars and written materials. The NUCDF e-mail and listservs were most commonly highlighted by focus group participants and as such, should be leveraged to circulate new evidence in the field. In addition to the NUCDF listserv, caretakers subscribed to several other rare-disease listservs that researchers may consider targeting, including the *National Organization of Rare Disease (NORD)*, the *NIH Rare Disease Network*, and *RareConnect*. Caretakers also mentioned sites sponsored by the pharmaceutical industry, such as the *Rare Disease Foundation*, *Rare Share*, and the *Rare Disease United Foundation*. It was not clear whether they knew the origins and sponsors of the information provided on these sites. Patients noted individual hospital listservs as a

“Maybe get on an email list or something. We can get emails from everybody about everything in the world. Why couldn’t we get [UCD] status news updates...Anything that comes up about it, UCD, you’ll get notification on it. Then you can go out and do that further research that we all do anyway. It gives us somewhere to go, know at least, hey, this has happened.”

– Caretaker Focus Group Participant

resource so researchers may also encourage hospital members of the UCDC network to distribute webinar information and written materials through their patient e-mail lists.

Social Media

Social media platforms, particularly Facebook, were cited as a common resource for patients and families. Posts in UCD-related Facebook groups were described as both a convenient and timely method for distributing new information to the wider UCD community. Some caretakers even preferred the more rapid exchange of information on sites like Facebook and Twitter to the e-mail and listservs. However, caretakers also described problems authenticating and validating information posted to these social media platforms and were not always able to assess the quality and strength of the information available through these groups. Researchers may consider promoting new findings, webinars, and newly developed written materials through UCD Facebook groups but should do so with care and caution. Researchers should aim to leverage Facebook groups managed through a transparent and trusted administrator, such as the NUCDF-administered Facebook group.

As several caretakers suggested, researchers should post links to external websites and documents that assist the Facebook user (the UCD patient or caretaker) in assessing the credibility of posted information.

“I feel like sometimes with emails, or newsletters, or anything... it feels not very timely. By harnessing the social media piece...it'd be a way to get it out there right away versus waiting for the next newsletter. I feel like today, everybody's just clamoring for information all the time...I'm clicking through my Twitter feed wherever I am...I can choose if I dive deeper and go into their website...I feel like those bits and pieces are easier to consume than a whole— a lot of information at a time.”

– Caretaker Focus Group Participant

Long-term Strategies Targeting Patients and Families

Centralized Website or Mobile App

Caretakers viewed the development of a centralized website as a favorable long-term strategy for dissemination of material related to UCD. They liked the idea of a central hub for vetted information, including links to new research publications and summaries, archived recordings of presentations and webinars, and other written materials. In addition to these contributions, caretakers suggested that the website host a collection of family-told medical and liver transplant patient stories (both positive and negative). Many caretakers described being influenced in treatment choice, at least in part, by other families' experiences with medical management and transplant. Most spoke only to a small number of other families with whom they were able to connect and felt they would have benefitted greatly from a larger repository of stories offering them a more balanced perspective.

"If we had a central location that we could put the information that is accessible—like the studies and the research papers...if there was a central location that we could put that stuff in...that would be just easier."

- Caretaker Focus Group Participant

Caretakers saw a mobile application as serving a similar purpose with more focus put on quick links and short summaries as well as tools that can be taken with them to physician appointments (e.g., "questions to ask my provider" checklist).

For a website or mobile application to retain its credibility and value, it must be consistently maintained and frequently updated so that the information reflects the most current developments in the field. Caretakers cited this as a chief complaint of other existing websites and internet information resources. Any centralized website or application developed for the purpose of UCD-related information dissemination should be done so with a long-term strategy for website administration and content management.

"The most important thing in a website, is that it's kept current. If I go to it, and then I'm looking at it, and clicking resources, and the last thing that they posted was something in 2014, then that just makes me wonder, is that the right place to go for information?"

- Caretaker Focus Group Participant

Under development: The NUCDF has secured additional resources not originally available through this study to develop a centralized website and application (app). The app will provide research updates and layman's briefs, links to publications, and summaries, among other useful features.

Local NUCDF Chapters and Peer Mentorship

Caretaker focus group participants suggested the development of local NUCDF chapters and/or a formal peer mentorship network as another long-term strategy for dissemination of information and experiences related to UCD. Caretakers place great value on the

“I love the idea of having local meeting sites...that can connect you face-to-face with other parents...I love the idea of having more localized groups.”

– Caretaker Focus Group Participant

experiences of others within their community and rely on the support and guidance of other families in navigating the treatment options available to them. Caretakers felt that a more formalized system for connecting families to others in their local network would help promote even

more communication within the community. This system would assist in the diffusion of new developments and evidence, provide families with mentorship support (i.e., guidance on the most helpful forms of information and credible resources available to share), and promote an institutionalization of existing knowledge by encouraging the development of local leaders and “expert mentors.”

Despite the challenges that are associated with the rarity of UCD, the NUCDF has been able to maintain a mentor program. This program matches families to mentors and then to a larger support network consisting of local support groups and activities once they have an understanding of the wide variability of the disorder and information as it applies to their child. “Chapters” require governance under specific nonprofit designations, which is a challenge for a smaller nonprofit, such as the NUCDF and other 501(c)(3) rare disease nonprofit organizations that have geographically dispersed patient populations. If the number of families is small (2-3 families), a formal chapter may not be feasible. The sample of focus group caretaker participants were not necessarily aware of the NUCDF’s mentorship program so some renewed efforts to publicize the program might be warranted.

Remote & Virtual Physician Consultations

Several caretakers described challenges in consistent access to expertise in metabolic care. Rare disease management is regionalized in nature, and expertise in UCD care is found predominantly in a few large, urban, academic settings. Remote or virtual physician consultations could be considered as a strategy to help address access deficits for families living far from these institutions. A telemedicine approach to UCD consultative care may help promote access to guidance from providers tied into the UCDC network whose practice may be more likely aligned with developing evidence in the field.

“If there was someone at the UCDC to just take a quick phone call or a chat email session...point you in the direction or give you additional resources and knowing that that’s coming from a professional source, I think something like that would be helpful.”

– Caretaker Focus Group Participant

Due to practical and legal obstacles, such an approach has been slow to develop at a national level. However, some providers do conduct regional visits and telemedicine through their own institutional partnerships.

Targeting Providers with New Information

Caretakers who cited their clinical providers as a key and trusted resource for information about UCD treatments were interested not only in the direct dissemination to UCD families, but also in the dissemination efforts that would be undertaken to reach physicians and other members of the care team when new evidence becomes available. Caretakers rely heavily on the guidance of their clinical care teams. Thus, in crafting a dissemination strategy that is responsive to the needs and priorities of UCD families, researchers must also consider metabolic, liver transplant, pediatric, and other relevant hospital providers as key targets for new findings in UCD care. The next several sections of this document outline various approaches that may be considered in the dissemination of UCD related evidence to this inclusive network of clinical providers.

Short-term Strategies Targeting Providers

Peer Reviewed Publications, Conferences, and Lectures

The most common short-term strategy for disseminating information on UCD treatment alternatives is through publications in peer-reviewed manuscripts and presentations at scientific conferences. Focus groups conducted with metabolic, hepatology, and transplant providers found that providers rely primarily on colleagues and traditional academic sources for information on UCD. Providers place high priority on information validity, citing the peer-review process as an important mechanism for quality assurance.

Metabolic providers cited *Molecular Genetics and Metabolism* and *The Journal of Inherited Metabolic Disease* as high-impact journals in their field. In contrast, transplant providers cited *Liver Transplantation*, *Pediatric Transplantation*, and *American Journal of Transplantation* as high-impact journals in their field. Reflecting the sentiments of many caretakers, focus group providers cited the lack of overlap in journal readership as one

“I think it’s challenging, because we don’t go – transplant physicians don’t go to metabolics [sic] conferences, and when you guys are mentioning the journals you read, I didn’t realize that those were the key journals. I wonder if you guys realize which publications or journals we read. We don’t kind of crosstalk very much. I think that’s the challenge, but as long as that’s recognized, and the authors of this research present the research to both groups, I think it’ll get the exposure it needs.”

-Hepatology Provider Focus Group Participant

contributor to lack of feedback between the metabolic and transplant physicians. Providers noted that a lack of shared information between specialties inhibits their ability to provide comprehensive counsel to patients regarding all treatment options. Providers agree on the importance of targeting new information on the two treatment alternatives in journals with high readership by general medical audiences – such as *Pediatrics*, *New England Journal of Medicine*, or *JAMA* – to maximize the likelihood that it reaches both the metabolic and liver transplant fields.

Using a multi-pronged dissemination approach is important to reach the greatest possible number of UCD providers. Providers suggested ways to increase traffic to publications that include important new information. Some ideas include highlighting new articles in journal editorials, disseminating to professional society members through listservs, and presenting findings at scientific conferences ahead of publication. Providers noted that while access to published information is important, obtaining new information from conferences is also effective. Well-attended conferences, in particular, were viewed by focus group participants as an important platform for practicing physicians to share and learn about the latest research in a timely manner. However, one disadvantage of relying solely on conferences to disseminate findings is that information can only be conveyed to those who attend each given presentation. Providers tend to gravitate towards conferences and

publications in their own fields, making it vital to target both conferences and journals accessed by providers in both fields, promoting a greater exchange of knowledge.

Notably, one provider proposed recorded and traveling lectures and/or webinars, ideally led by providers from both fields, as a more novel dissemination strategy that would bypass the shortcomings of traditional scientific meetings. This approach would allow for more participation among a wider audience that could cumulate over time. This strategy could be implemented in the midterm, potentially within medical institutions (in the form of grand rounds) and through professional liver and metabolic societies.

“Either creating a presentation that we could download and present at our own institutions or just create a lectureship where we identify somebody who’s prepared a presentation on this subject. Maybe you create a lecture with a metabolic geneticist and a transplant doctor and have these two people...repeat the lecture at multiple centers.”

– Provider Focus Group Participant

Under development: The NUCDF is preparing webinars, presentations, and educational modules (some in partnership with the UCDC).

Long-term Strategies Targeting Providers

Literature Reviews, Clinical Guidelines, and Practice Parameters

A longer-term strategy to disseminate evidence on UCD treatment alternatives that builds on the existing academic infrastructure is synthesizing findings from rigorous studies in

“One of the things I find very helpful in guidelines and reviews are the references so that, if I want, I can go to the original reference to understand where that recommendation came from.”

– Provider Focus Group Participant

the form of both reviews and clinical guidelines. Reviews and clinical guidelines are convenient for providers to access existing vetted evidence on UCD treatments in a centralized and digestible manner. Furthermore, reference lists from published reviews and clinical guidelines provide a comprehensive

compilation of articles that providers can easily use to locate the source studies from which any given piece of information or recommendation comes from. Literature reviews, however, are intensive

endeavors that typically demand the coordinated efforts of a team of trained researchers and clinicians and would likely require substantial funding to pursue. Because literature reviews are outdated as new studies are published, deliberate efforts to update literature reviews would be required to ensure that they remain a reliable source of UCD treatment information. This need for updates means that relying on *ad hoc* initiatives from

“I will say that I think it’s very hard to standardize things across the country. There so many local factors that can play into the care that somebody might receive. I think you can—I think it’s helpful to set parameters, but I think it’s hard to standardize things completely across the country.”

– Provider Focus Group Participant

“The guidelines also give us some edge when we’re making our transplant policies or maybe our departmental metabolic policies as a group. If you want to say, as a group, let’s all tend to manage a condition a certain way, if it’s in the guidelines, it gives that policy some clout...Making sure that they’re in the guidelines and the guidelines are up-to-date gives the policymakers for each program some clout in saying, well, it’s part of the guidelines, we should be doing it standard of care, and I think that’s key.”

– Provider Focus Group Participant

individual researchers or institutions would likely be insufficient. The task of updating clinical guidelines – which according to our focus group providers, were last updated in the early 2000’s – is even more challenging. While the sentiment in our focus groups was that updated clinical guidelines would theoretically be beneficial to both providers and patients, many providers questioned whether developing standard guidelines was a realistic, or even desirable goal given the wide variations that exist in UCD treatment approaches.. One physician noted that each of the several institutions that she

has worked in has its own approach to managing UCD. However, these provider perspectives perhaps underscore the potential positive impact that standard evidence-based clinical recommendations may have on patient outcomes.

Many agreed that the current evidence is not sufficient to warrant hard, prescriptive guidelines that present a ‘single best way,’ and that a set of evidence-driven practice parameters or standards may be more attainable. Less prescriptive guidelines would also be more useful for adapting to the resources and infrastructure of different locales and institutions. A focus group transplant provider noted clinical guidelines as an important resource when crafting departmental policies. Clinical guidelines provide policy makers with ‘clout’ in justifying new practices and standards. The lack of up-to-date clinical guidelines may be especially problematic for more policy-driven departments and institutions to continue updating their own internal policies.

Under development: The NUCDF and the UCDC are currently updating and developing practice guidelines and resources. Clinical experts serve on working groups, including one focused on liver transplant. Families were able to provide input via surveys and a “*Developing Clinical Practice Resources-Patient & Caregiver Perspectives*” focus group conducted at the NUCDF Annual Family Conference.

Centralized Website or Mobile App

A centralized website and a mobile app are popular ideas as a potential source of information dissemination among UCD caretakers but not among providers. Many

“Having a website is, I think, at least for the providers, it’s—yeah, some people will go to a website, some people won’t, but nobody can argue against a publication.”

– Provider Focus Group Participant

providers noted that setting up another website may not be useful for disseminating information more widely. Providers indicated that they already have multiple websites that they visit to obtain new information, including *clinicaltrials.gov*, the NUCDF website, the Rare Disease Clinical Research Network, and the UCDC website.

Compared to caretakers, providers expressed greater concern over the ownership of the new website. In particular, they were concerned about the implications of website ownership on the types of information that would be presented, as well as the reliability with which it would be synthesized or summarized, recognizing the subjectivity and the lack of

“I think one of the real tricky parts about the website is making sure that it’s balanced in terms of information. It’s easy to say, transplant is so great, here’s all the great things about it, or to paint a really dire picture...because clinicians have such different opinions about it... one of the challenges would be to really make sure that it’s balanced and that it’s not pushing people to one or the other.”

– Provider Focus Group Participant

accountability inherent in publishing content on the web. Providers noted the inherent challenge of ensuring that the information presented on a new website is transparent, as many studies of treatment outcomes are conducted or sponsored by pharmaceutical companies.

Some providers were enthused and optimistic about the idea of an easily-referenceable mobile app for UCD treatment information. A mobile app could be a useful tool for counseling patients in settings where a computer is not available. However, most were more skeptical about the usefulness of an app for the purposes of obtaining information in general, and especially for UCD treatment information due to the complex nature of the topic. Providers similarly articulated concerns over the ability to keep information up-to-date in an app. Nevertheless, providers were generally more favorable toward an app geared toward facilitating UCD management (e.g., by containing calculators and other tools) rather than one tailored solely for presenting information.

Under development: The NUCDF has secured additional resources not originally available through this study to develop a centralized website and app. This app will provide research updates, layman's briefs, links to publications, and summaries, among other useful features. In addition, a diet management app and other tools/calculators are being validated and prepared for formal release to the UCD patient and research community.

IMPLEMENTATION OF DISSEMINATION SOLUTIONS

The short-term dissemination strategies discussed in this document can be reasonably executed through the existing collaboration between the NUCDF, Children's National Health System (CNHS), The George Washington University (GW), and The Studies of Pediatric Liver Transplantation (SPLIT). This PCORI-funded study compares the effectiveness of medical management and liver transplant as treatment for UCD and explores the treatment decision-making experiences of UCD families. Multiple methods for dissemination of study results should be explored. These methods should include presentation via patient conferences/webinars, peer-reviewed and layman-generated written materials, information presented through email, listservs, and social media, and the strategic placement of presentation and publications aiming to capture a wider clinical audience. Most of these strategies can build upon the existing work of the NUCDF.

While longer-term patient and provider level dissemination strategies discussed in this document may fall outside the scope of this study, several are already being undertaken by the NUCDF. Insights from provider and patient participants on the value of these approaches should be considered as the current dissemination efforts are finalized and future dissemination interventions are developed. The continued or new development of a centralized website, local advocacy chapters, literature reviews, new practice parameters, a traveling and/or recorded lecture series, or a platform for remote/virtual UCD physician consultation will require additional resources and extensive planning. Additional planning will include developing a strategy for the long-term sustainment of any of these implemented dissemination solutions. Any combination of the above listed long-term dissemination strategies may be considered ripe for piloting and evaluation, including the identification and development of metrics to assess their efficacy as a vehicle for the distribution and uptake of new evidence and information.

CONCLUSION

This dissemination strategy was written in direct response to qualitative data collected from both the caretakers of children diagnosed with UCD and clinical providers. The qualitative data was collected by GW for a PCORI-funded study titled Comparative Effectiveness of Therapy in Rare Diseases: Liver Transplantation vs. Conservative Management of Urea Cycle Disorders. This study was developed through a close partnership between the NUCDF and the UCDC. The dissemination challenges and approaches outlined in this document represent the needs and priorities of patients and families. In addition, this document outlines the information sharing preferences of UCD providers, as they were expressed through in-depth focus groups and interviews devoted to the use of information and how best to convey evidence in order to meet expectations. Implementation of any of the above described dissemination efforts should be done in direct collaboration with patients and families through the NUCDF, who will continue to engage members of the UCD community in the development, finalization, and distribution of dissemination materials.