MAPPING THE RARE CAREGIVER JOURNEY

May 7, 2022

Hypoxic-Ischemic Encephalopathy (HIE)

This multiphase research aims to understand the complexity and nuances of the caregiver experience for individual diagnoses and their impact on mental health and emotional well-being to inform a curriculum that enables mental health professionals to deliver aligned and informed individual and peer support.

Correspondence:

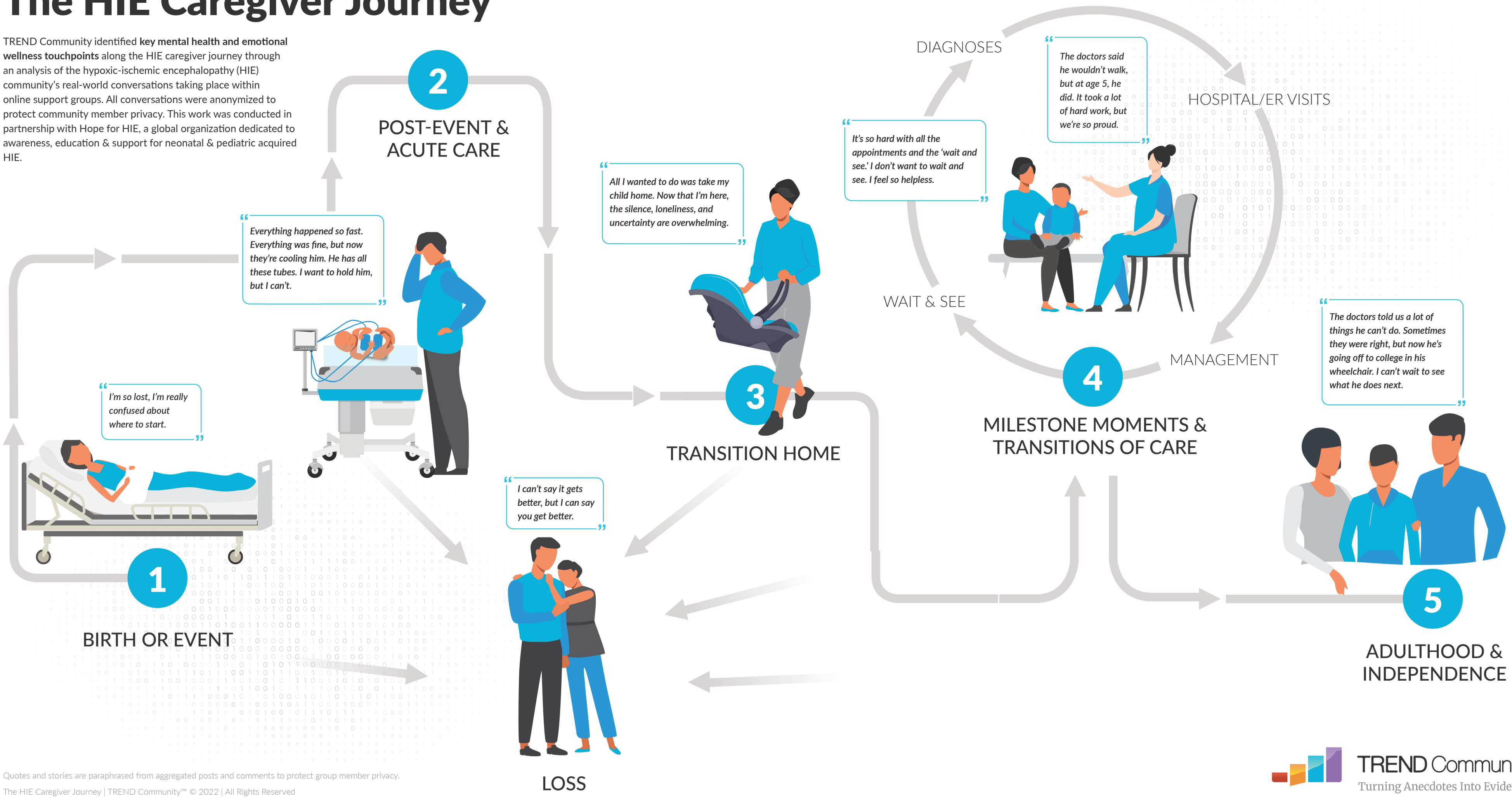
Maria Picone, CEO

maria@trend.community

TREND Community

The HIE Caregiver Journey

TREND Community identified **key mental health and emotional wellness touchpoints** along the HIE caregiver journey through an analysis of the hypoxic-ischemic encephalopathy (HIE) community's real-world conversations taking place within online support groups. All conversations were anonymized to protect community member privacy. This work was conducted in partnership with Hope for HIE, a global organization dedicated to awareness, education & support for neonatal & pediatric acquired HIE.



1 BIRTH OR EVENT

"I'm so lost, I'm really confused about where to start."

2 POST-EVENT & ACUTE CARE

"Everything happened so fast. Everything was fine, but now they're cooling him. He has all these tubes. I want to hold him, but I can't."

3 TRANSITION HOME

"All I wanted to do was take my child home. Now that I'm here, the silence, loneliness, and uncertainty are overwhelming."

4 MILESTONE MOMENTS & TRANSITIONS OF CARE

DIAGNOSES

HOSPITAL/ER VISITS

MANAGEMENT

WAIT & SEE

"It's so hard with all the appointments and the 'wait and see.' I don't want to wait and see. I feel so helpless."

"The doctors said he wouldn't walk, but at age 5, he did. It took a lot of hard work, but we're so proud."

5 ADULTHOOD & INDEPENDENCE

"The doctors told us a lot of things he can't do. Sometimes they were right, but now he's going off to college in his wheelchair. I can't wait to see what he does next."

LOSS

"I can't say it gets better, but I can say you get better."

Quotes and stories are paraphrased from aggregated posts and comments to protect group member privacy.

TREND Community™
Turning Anecdotes Into Evidence™

CONTENTS

INTRODUCTION

Rare diseases pose significant challenges not only to the individuals living with these conditions but also to those who care for them. It is estimated that there are more than 10,000 rare diseases,[1] and although previous research has identified common touchpoints along the caregiver journey, there is a wide degree of clinical heterogeneity among these diseases. Therefore, this multiphase research aims to understand the complexity and nuances of the caregiver experience for individual diagnoses and their impact on mental health and emotional well-being to inform a curriculum that enables mental health professionals to deliver aligned and informed individual and peer support.

In May 2019, TREND Community partnered with the foundation Hope for HIE (HFH) to turn the community's conversations into actionable insights. In 2011, HFH's founder, Betsy Pilon, created an online network of caregivers of children affected by HIE. This community has self-organized into groups that reflect different stages of the caregiver journey. The results from our analysis were documented in the Hypoxic-Ischemic Encephalopathy Community Voice Report (included in the appendix of this report).

OUR TECHNOLOGY

TREND Community harnesses machine learning and natural language processing techniques using Krystie$_{\text{TM}}$, our proprietary analytics engine, to capture the perspective and experiences shared online by people living with rare and chronic diseases.

Krystie was the daughter of one of our community members and the inspiration driving everything we work toward. Krystie, and the millions of others facing rare, chronic, and emerging diseases, are always at the heart of TREND Community.

LITERATURE OVERVIEW

OVERVIEW OF CAREGIVER STRESS AND BURDEN

Caregivers of patients with hypoxic-ischemic encephalopathy (HIE) undergo high levels of acute stress at the time of the birth/event and during the post-event/acute care period. In most cases, the event unexpectedly occurs at birth, leaving parents filled with shock, fear, anguish, anger, disbelief, and devastation, and putting them at substantial risk for post-traumatic stress disorder (PTSD).[2-5] During the birth/event and post-event/acute care stage, parents who are now caregivers to their injured infant or child are especially vulnerable; clinicians and nonclinical staff must consider an empathetic and measured approach to prevent additional traumatization and retraumatization of the caregivers.

Caregiver stressors involve direct care of the recipient, such as bathing, lifting, administering medications, and transporting the patient to and from medical appointments. Additional strains from financial pressures; relationships with other children in the household, coworkers, and friends; and intrapsychic strains, such as isolating behaviors, depression, and anxiety, can lead to role engulfment. As caregivers strive to meet the demands of caring for the individual with HIE and fulfill other roles in their lives, the stressors can negatively impact both their mental and physical health.[6] Risk factors for caregiver burden include female sex, having no choice in being in the caregiver role, lower education attainment, limited financial resources, limited self-care, insufficient psychosocial support, and 24/7 care expectations.[7]

A survey conducted on participants in the HIE community identified key themes that were relevant to communication and parental involvement during their stay in the neonatal intensive care unit (NICU). Themes identified were the setting for communication, content/clarity of language, immediate and longitudinal support, clinician time and scheduling, valuing the parent role, and physical presence and touch.[8] These themes closely align with the Substance Abuse Mental Health Services Administration's (SAMSHA's)[9] principles of a trauma-informed care approach for interacting with caregivers. These strategies have been applied in many different settings. The 6 principles are safety; trustworthiness and transparency; peer support; collaboration and mutuality; empowerment, voice, and choice; and cultural, historical, and gender issues.

Sanders[10] laid out a plan for the NICU, implementing SAMHSA's principles for trauma-informed care with applications derived from the Interdisciplinary Recommendations for Psychosocial Support of NICU Parents[11] and Trauma-Informed Care in the NICU.[12] The types of strategies in the plan include reuniting the family as soon as possible after the birth or traumatic event; allotting privacy in single-family rooms; medical professionals providing clear, concise language that is free of medical jargon and using empathetic tones; allowing parents access to medical records; allowing the parents' presence during rounds; offering peer-to-peer support; nurses taking the role of mentor and letting the parents participate in care activities; parents being supported and encouraged in their role; and making sure that all families feel welcomed and are treated equally with culturally effective care.[10]

The intense nature of the caregiver's role lends to extreme stress and conflict for parents and guardians in the HIE community. As role engulfment ensues, the caretaker can experience mental illness, physical illness, sleep deprivation, and fatigue from the impact of stress and care burden as they strive to meet the demands of both caring for individuals with HIE and maintaining their other responsibilities and interpersonal relationships. Implementing trauma-informed care principles in the healthcare setting will enable caregivers to receive the support and understanding needed to obtain the best mental health support for themselves so the best care can be afforded to the patient.

The full literature review is included in the appendix of this report.

DATA SOURCES

Real-world conversation data from the following closed online support groups were included in our analysis. Data were analyzed with permission from the group administrator.

Hope for HIE Support Parent Hub (7.3k members)
Main hub of HFH parent support forums connecting families of children diagnosed with HIE from around the world.

New to HIE (501 members)
For parents who are still in the very early days of HIE, be that in the NICU, post-HIE event, or soon after discharge from the hospital.

The In Between in HIE (1k members)
For parents whose children are developing within a typical developmental range, or have mild or moderate impacts from HIE, who are more than 1 year old or 1 year postinjury.

More Severe Outcomes (664 members)
A support group for parents or guardians of a child who has more severe impairments as a result of HIE.

Pregnancy after HIE (1.1k members)
For mothers who want to discuss the ins and outs and complexities of pregnancy after HIE.

Other Data Sources

The following groups may be targeted for future analysis:

- HIE Dads
- HIE Acquired in Childhood
- Adoptive & Foster Families
- Loss Support for Parents
- Self-Care for Parents

HIE CAREGIVER JOURNEY MAP

TREND Community identified key mental health (MH) and emotional wellness (EW) touchpoints along the HIE caregiver journey through an analysis of the HIE community's real-world conversations taking place within online support groups. All conversations were anonymized to protect community member privacy. This work was conducted in partnership with Hope for HIE, a global organization dedicated to awareness, education, and support for neonatal and pediatric acquired HIE.

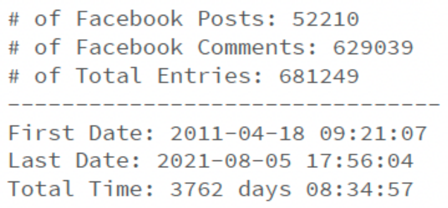
TOUCHPOINTS IDENTIFIED

- Birth or Event (eg, near drowning)
- Post-Event & Acute Care (eg, NICU)
- Transition Home
- Milestone Moments (eg, developmental milestones such as walking or birthdays) & Transitions of Care (eg, early intervention to kindergarten)
- Adulthood & Independence (a spectrum of experiences)
- Loss (eg, loss of hopes and dreams or death of loved one)

The diagram on the next page visually depicts these touchpoints. The team also identified a series of recurring events during stage 4 of the journey that present MH and EW challenges and opportunities for MH providers and peer support (Hospital/ER Visits, Diagnoses, Wait & See [anticipation of what is to come], and Management).

SOCIAL DATA OVERVIEW

Hope for HIE Support Parent Hub (7.3k members)

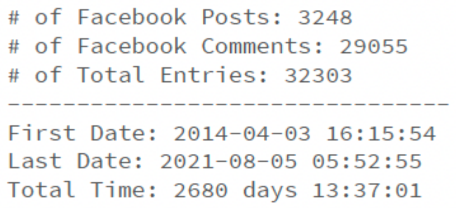


```
# of Facebook Posts: 52210
# of Facebook Comments: 629039
# of Total Entries: 681249
--------------------------------
First Date: 2011-04-18 09:21:07
Last Date: 2021-08-05 17:56:04
Total Time: 3762 days 08:34:57
```

New to HIE (501 members)

```
# of Facebook Posts: 7798
# of Facebook Comments: 67619
# of Total Entries: 75417
--------------------------------
First Date: 2014-08-20 19:15:30
Last Date: 2021-08-03 15:41:12
Total Time: 2539 days 20:25:42
```

The In Between in HIE (1k members)



```
# of Facebook Posts: 3248
# of Facebook Comments: 29055
# of Total Entries: 32303
--------------------------------
First Date: 2014-04-03 16:15:54
Last Date: 2021-08-05 05:52:55
Total Time: 2680 days 13:37:01
```

More Severe Outcomes (664 members)

```
# of Facebook Posts: 2217
# of Facebook Comments: 19574
# of Total Entries: 21791
--------------------------------
First Date: 2014-04-03 18:13:28
Last Date: 2021-08-03 04:07:19
Total Time: 2678 days 09:53:51
```

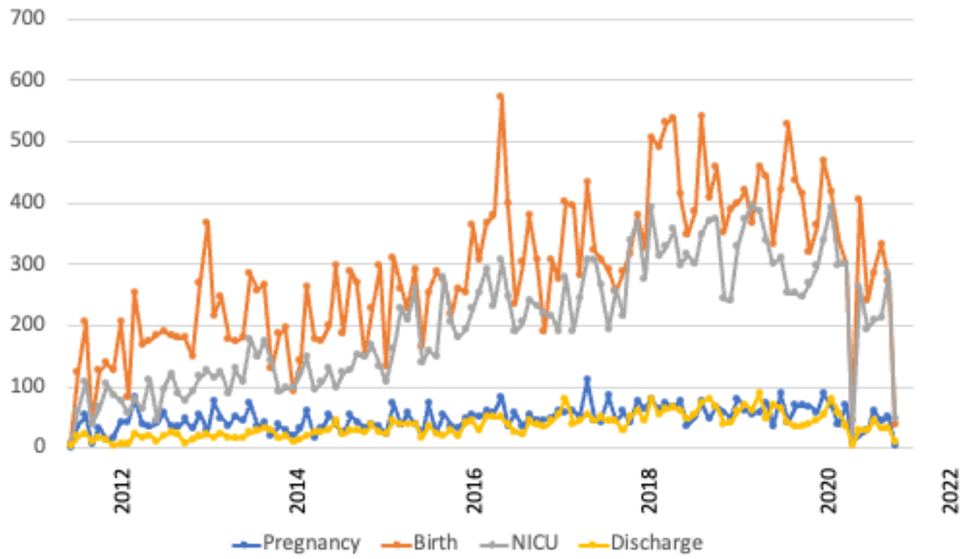
Pregnancy after HIE (1.1k members)

```
# of Facebook Posts: 4118
# of Facebook Comments: 42536
# of Total Entries: 46654
--------------------------------
First Date: 2013-12-07 23:24:49
Last Date: 2021-08-03 01:18:38
Total Time: 2795 days 01:53:49
```

EARLY STAGES

“New to HIE” and “Parent Hub” were collapsed to evaluate the beginning stages of the caregiver journey: **pregnancy**, **birth**, **NICU**, and **discharge**. We see that **birth** consistently is the topic of greatest frequency, followed by **NICU**, **pregnancy**, and **discharge**. The following graph (Figure 1) depicts the amount of conversation by topic over time. **Pregnancy** posts/comments totaled 5670 (0.07% of all data), **birth** totaled 33,221 (4% of all data), **NICU** totaled 23,475 (3% of all data), and **discharge** totaled 4197 (0.05% of total data). The gap in the data represents a period during which we were unable to collect conversation data from the groups because of Facebook application issues.

Figure 1. Early Stages Discussion Time Series



MENTAL HEALTH

We used Krystie to identify discussions in the early stages of the caregiver journey that were related to MH and isolated statements with a high probability (>0.80) of discussing MH (approximately 10% of all statements in Early Stages).

Mental Health Language

Figure 2 graphs depict the frequencies for MH terms (eg, anxiety, depression) in conversations for each subgroup after isolating high-MH statements.

Pregnancy (4317 total statements):

- Highest Term: approximately 7% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 2% of all statements mentioned a 'depression' term

Birth (19,849 total statements):

- Highest Term: approximately 3% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 1% of all statements mentioned a 'depression' term

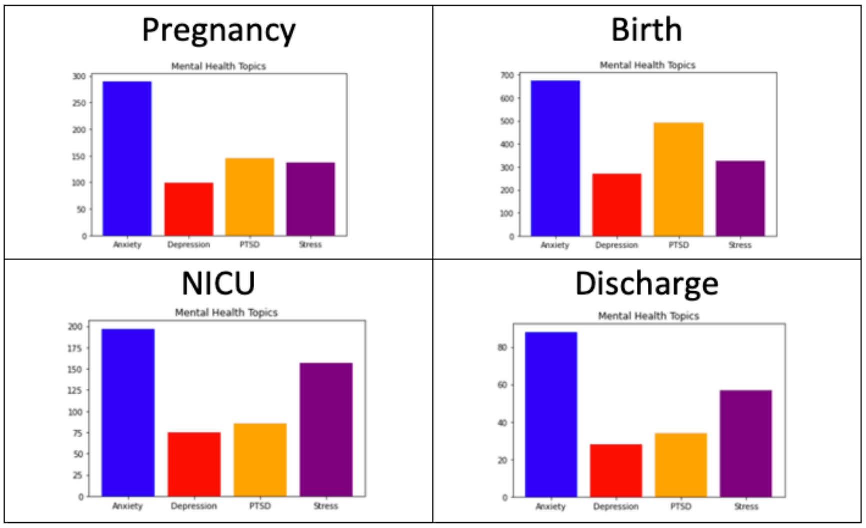
NICU (9448 total statements):

- Highest Term: approximately 1% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 0.06% of all statements mentioned a 'depression' term

Discharge (4347 total statements):

- Highest Term: approximately 1% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 0.01% of all statements mentioned a 'ptsd' term

Figure 2. Mental Health Language by Subgroup



Emotional Language

With some understanding of the kinds of high-frequency terms that exist in the data, we can also start to understand the emotional affect of statements by exploring "emotional weights" of MH-related conversations in each group (Figure 3).

Pregnancy (41,495 total words):

- Highest Weight: approximately 8% of all words were weighted on 'anticipation'
- Lowest Weight: approximately 4% of all words were weighted on 'disgust'

Birth (183,713 total words):

- Highest Weight: approximately 8% of all words were weighted on 'fear'
- Lowest Weight: approximately 3% of all words were weighted on 'disgust'

NICU (88,043 total words):

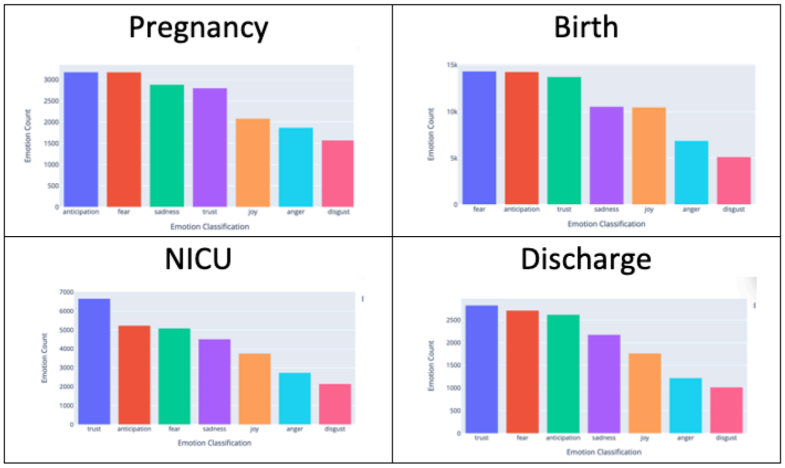
- Highest Weight: approximately 8% of all words were weighted on 'trust'
- Lowest Weight: approximately 2% of all words were weighted on 'disgust'

Discharge (40,559 total words):

- Highest Weight: approximately 7% of all words were weighted on 'trust'
- Lowest Weight: approximately 3% of all words were weighted on 'disgust'

We see early on that *anticipation*, *fear*, and *sadness* are most prevalent. *Fear* and *anticipation* remain high in birth, while *trust* grows in relative contribution. When we get to the NICU and discharge experience, *trust* becomes the most prevalent affect in statements. This relates to previous analysis with topics including *don't know* and *not knowing*. The following graphs depict the emotional weights of conversations in each subgroup.

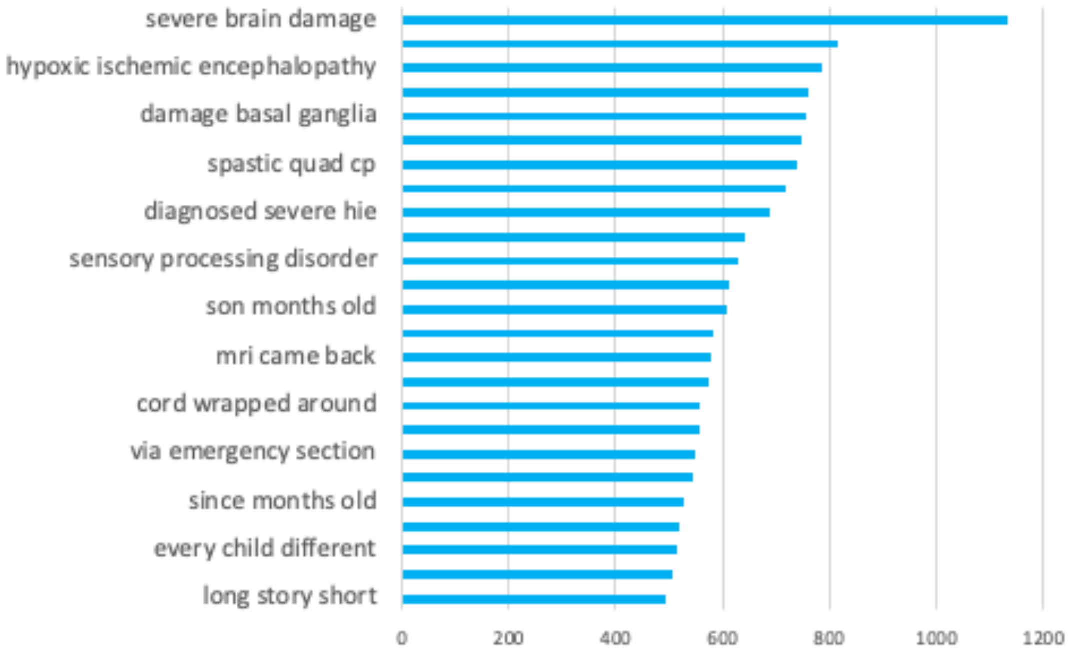
Figure 3. Emotional Weights of Conversations by Subgroup



Most Frequent Terms

Following a >0.80 score cutoff for likelihood of discussing 'mental health,' three-word combinations were selected to illuminate descriptive elements of the phrases (eg, *severe brain damage*, *damage basal ganglia*, *never walk talk*) (Figure 4). This resulted in approximately 230,00 sentences to calculate phrase counts.

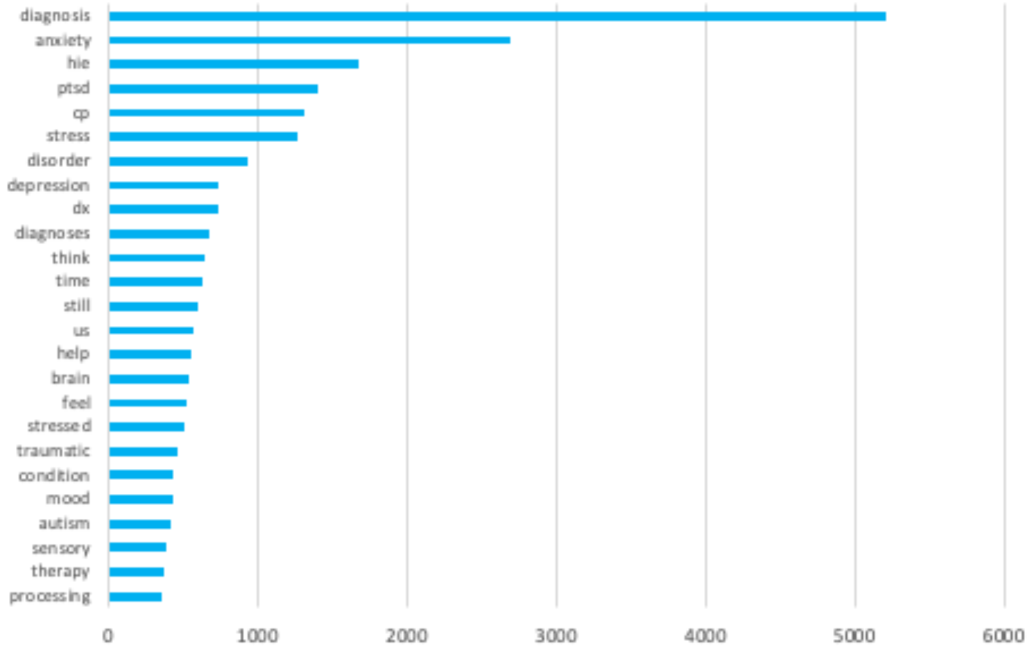
Figure 4. Top 3-Word MH-Related Phrases



Diagnosis Language

Following a >0.80 score cutoff for likelihood of discussing 'mental health,' we filtered for statements that mentioned terminology related to diagnosis. This included 6% (approximately 15,700 sentences) of all high-MH statements. The following graph (Figure 5) displays the top MH-related words that were identified by Krystie from conversations determined to be about diagnoses.

Figure 5. Top MH-Related Words About Diagnoses

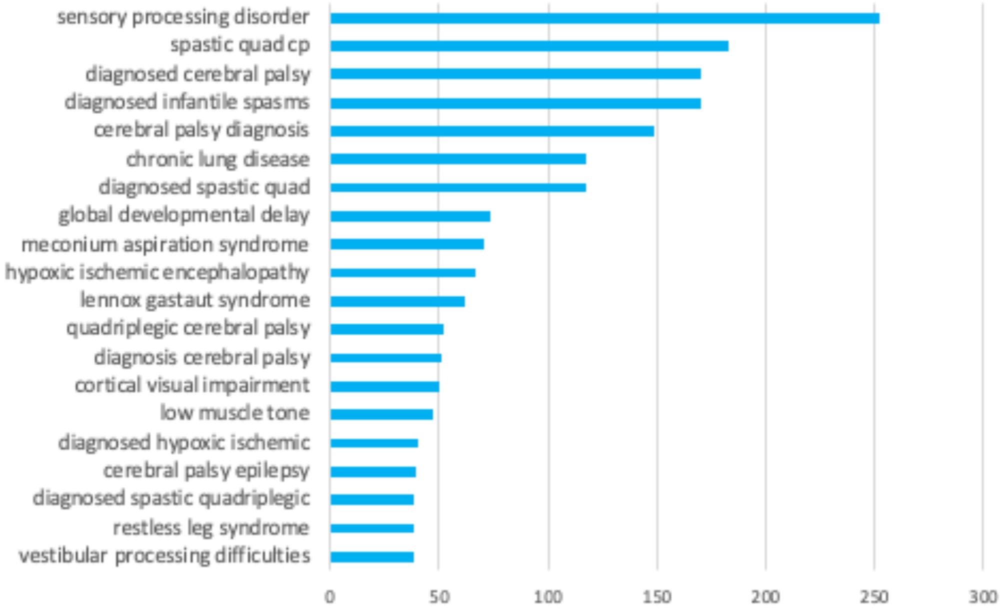


Legend: *dx* - diagnosis; *cp* - cerebral palsy; *ptsd* - post-traumatic stress disorder

HIGH MEDICAL DIAGNOSES/DISORDERS

We used Krystie to identify discussions in the early stages of the caregiver journey that were related to medical diagnoses and disorders (approximately 1% of all statements remained following the isolation of statements using 'diagnostic' language). Three-word phrases were selected to offer full diagnosis names (eg, sensory processing disorder, meconium aspiration syndrome) vs 1-word terms (eg, disorder, syndrome) (Figure 6).

Figure 6. Top 3-Word Diagnosis Phrases



MIDDLE STAGES

To offer a broad understanding of the caregiver journey through early adolescence, we conducted a focused analysis of 2 groups: "The 'In Between' in HIE" and "More Severe Outcomes."

Milestones

In both groups, discussion around ages and milestones appears to be prevalent (eg, *years old*, *months old*, *12 months*, *15 months*) (Figures 7,8). We see that the relative number of posts/comments decreases with increasing age in More Severe, whereas frequencies are similar from *0-24 months* in In Between. The highest frequency in More Severe is *0-6 months*, and is *school age* in In Between. For More Severe, the highest-frequency bin (*0-6 months*) accounted for approximately 1 out of every 200 posts/comments. For In Between, the largest bin (*school age*) accounted for approximately 1 out of every 125 posts/comments.

Figure 7. Milestone-Related Topics in More Severe

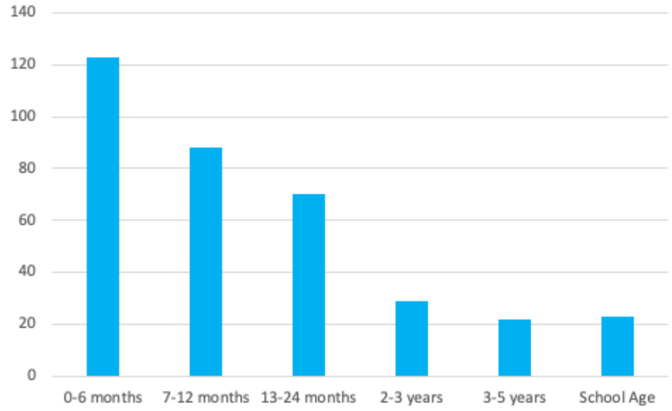
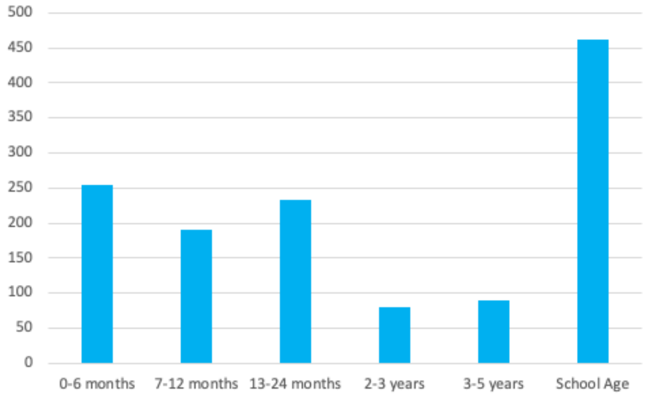


Figure 8. Milestone-Related Topics in In Between

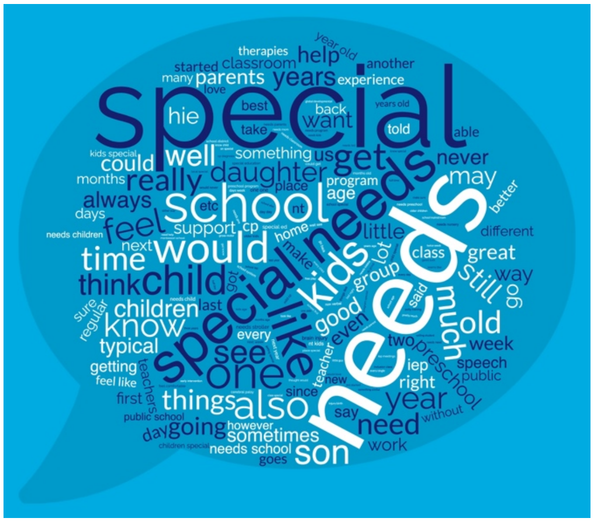


Special Needs

Through a topic-based machine learning approach, TREND identified topics/themes present in the More Severe and In Between data sets (Figures 9,10). “Special needs” was revealed to be a common topic in both data sets. To understand special needs in each group, we created a word cloud based on word frequency. One difference between groups is the size of school-based terms. In More Severe, these terms are smaller and more peripheral. Further, More Severe appears to have more medical-based language (eg, *medical*, *hospital*).

Figure 9. Special Needs Themes in More Severe

Figure 10. Special Needs Themes in More In Between



Mental health

Using Krystie, we isolated statements that were most related to mental health (approximately 10% of all data available). *Anxiety* and *stress* mentions are relatively high in More Severe, whereas anxiety tends to be dominant in In Between (Figures 11,12).

More Severe (6148 total statements):

- Highest Term: approximately 1% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 0.01% of all statements mentioned a 'ptsd' term

In Between (15,174 total statements):

- Highest Term: approximately 3% of all statements mentioned an 'anxiety' term
- Lowest Term: approximately 0.01% of all statements mentioned a 'depression' term

Figure 11. Mental Health Topics in More Severe

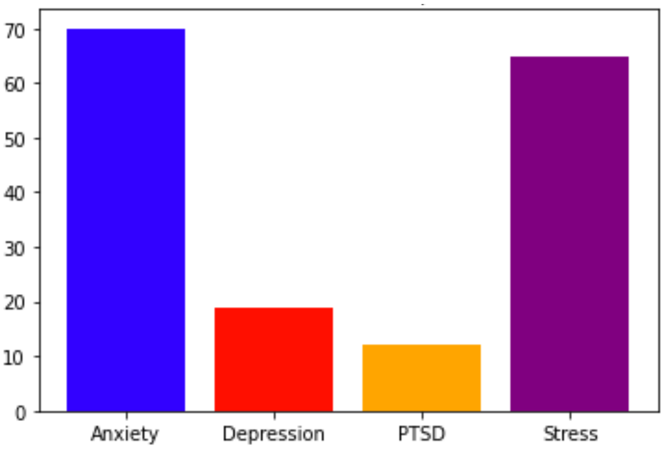
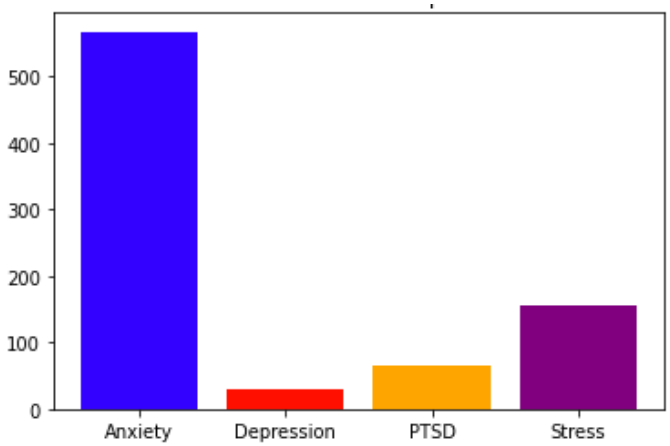


Figure 12. Mental Health Topics in In Between



Finances

Using Krystie, we isolated statements that were most related to finances (>0.80 probability score; approximately 1% of all data available). The highest 2-word combinations are provided for each group. *Insurance cover* is most frequent (approximately 1 in every 100 statements) in More Severe, whereas *school district* is most common (in approximately 1 in every 100 statements) in In Between (Figures 13,14).

Figure 13. Finance Topics in More Severe

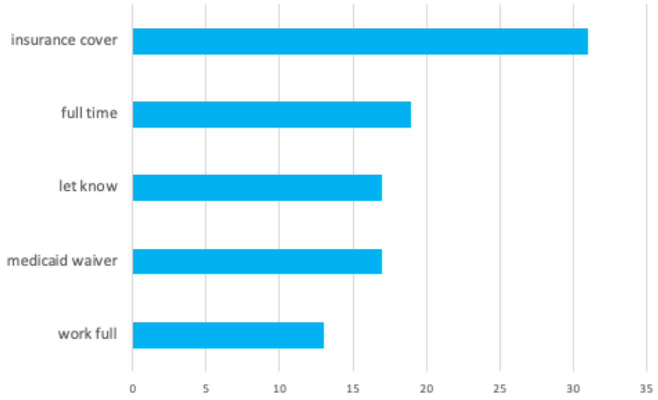
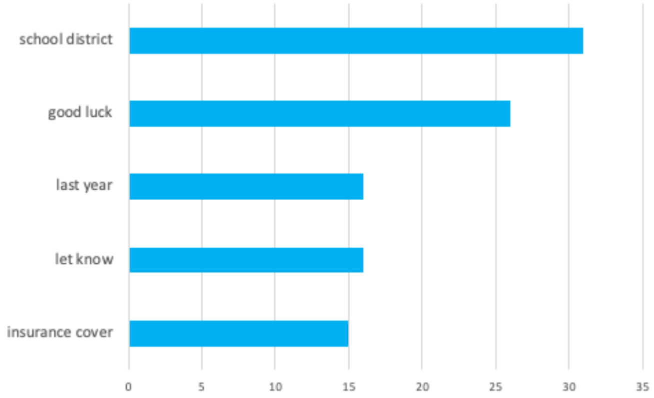


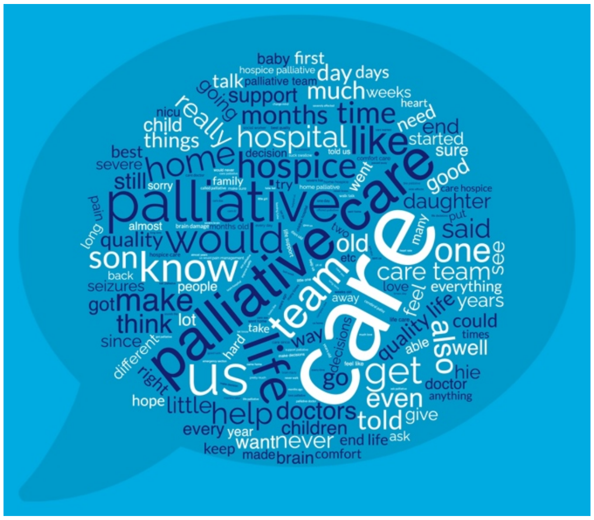
Figure 14. Finance Topics in In Between



Palliative Care (21,327 total words)

Using a topic-based machine learning approach, TREND Community identified topics/themes present in the More Severe and In Between data sets. One prevalent therapeutic intervention emerged in More Severe: palliative care. To further investigate this term, we isolated statements from "Parent Hub" and More Severe that discussed palliative care (approximately 500 posts/comments total) (Figure 15). The word cloud below shows the most frequent language used in these posts/comments.

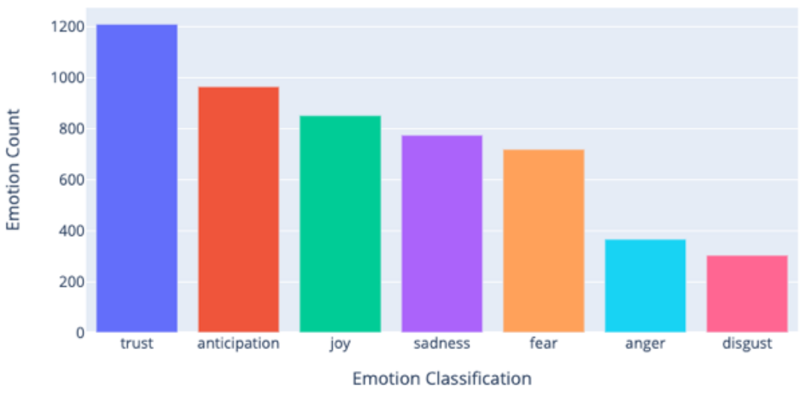
Figure 15. Palliative Care Themes



Words were then tagged based on their emotional affect. The emotional affect associated with those statements is plotted below (Figure 16). Words in palliative care statements were weighted the most on *trust* and *anticipation*.

- Highest Weight: approximately 5% of all words were weighted on 'trust'
- Lowest Weight: approximately 1% of all words were weighted on 'disgust'

Figure 16. Palliative Care Emotional Affect



Early Intervention (176,489 total words)

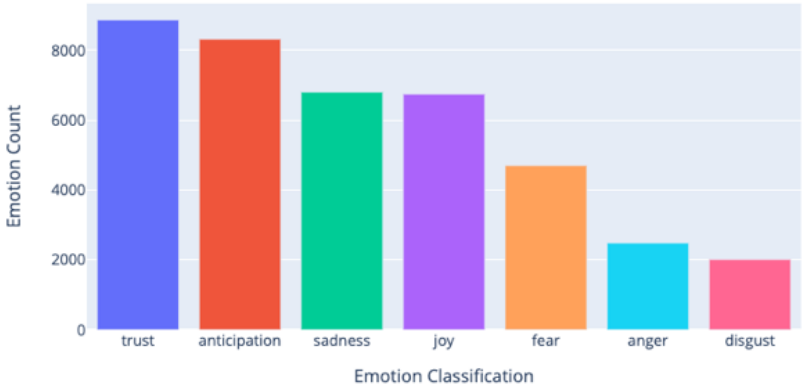
Using a topic-based machine learning approach, TREND Community identified topics/themes present in the More Severe and In Between data sets. One prevalent therapeutic intervention, *early intervention*, emerged in In Between. To investigate this term further, we isolated statements from "Parent Hub" and "In-Between" that discussed early intervention (approximately 3600 posts/comments). The word cloud below shows the language used most frequently in these posts/comments (Figure 17).

Figure 17. Early Intervention Themes

Words were then tagged based on their emotional affect. The emotional affect associated with those statements is plotted below (Figure 18). Like palliative care, words in early intervention statements were weighted the most on *trust* and *anticipation*.

- Highest Weight: approximately 5% of 176,489 total words were weighted on 'trust'
- Lowest Weight: approximately 1% of 176,489 total words were weighted on 'disgust'

Figure 18. Early Intervention Emotional Affect



PARAPHRASED STORIES

The following stories depict the experiences, sentiments, and needs identified at each touchpoint of the HIE caregiver journey. To protect the privacy of members of the community, TREND does not quote directly; instead, we write stories that reflect an amalgamation of the community experience.

Armando's Story (Birth or Event)

From the moment I found out we were expecting, my mind raced with the possibilities. Would the baby be a boy or a girl? Would the baby be healthy? My mind would daydream about playing ball with my child, about looking at the world through the eyes of a child. When my partner said, "he's coming," my heart swelled with joy and my body tingled with excitement.

I don't remember the words the doctor said, but I do remember the feelings and the questions. What is HIE? How did it happen? What does the future hold for my family? The curtain of grief dropped hard and fast. As hard as it was, and as hard as it will be, when I hold my son, there is love I never knew was possible."

Priya's Story (Post-Event & Acute Care)

It's hard to even put into words how much has changed even in the last day. A week ago, my pregnancy was uneventful . . . but then when my daughter was born, the cord was wrapped around her neck. So many doctors and nurses rushed in, and they whisked her away from me. They said they were going to cool her down, but I didn't really understand it at the time. Now I've done research and know all about it. I've been here in the NICU everyday as early as they let me in and as late as they let me stay. Everyone keeps telling me I need to take time to recover and take care of myself, but I don't want to be away from her. This is my child, and she needs me now more than ever. What if something happens again when I'm not here?

Mei’s Story (Transition Home)

As hard as it was navigating through the initial diagnosis and time in NICU, my husband and I were surrounded by medical professionals. The team at the hospital walked us through using the G-tube, the medications, and what to do when something unexpected happened. That information helped us prepare for what was ahead, but once we were at home, we were alone with our new “normal.”

When we were in the hospital, our thoughts were constantly on finally going home. But as great as it felt to be at home, it was the beginning of different challenges. The whirlwind of alarms, alerts, hospital announcements, and nurse check-ins were gone. That cacophony was replaced by the silence of our thoughts and the responsibility of caring for our child on our own. When they cried out, we were the only ones to respond. The loneliness and isolation were overwhelming, to say the least.

Jasmine’s Story (Milestone Moments & Transitions of Care)

Settling into our routine of treatments, appointments, scares, and flares took time. There were so many days when my partner and I held each other up. We would take turns staying positive and encouraging each other. The uncertainty of the future and our child’s delayed development weighed heavily on both of us.

The doctors told us our daughter would be developmentally delayed and that some traditional milestones might not be possible. She was 3 when she first told her moms, “I love you.” There are no words to describe the feelings that accompanied that moment. At 5, our sweet girl took her first steps; her excitement during that achievement still brings tears to our eyes.

Our daughter’s happiness and health will always be our goal. Seeing her grow according to her own timeline has been hard, but there is no greater joy than watching her journey.

——

Betty’s Story (Loss)

Appointments, therapies, treatments, smiles, and tears. The ups and downs of raising a child impacted by HIE can feel like a rollercoaster. There were so many questions after her diagnosis. There were so few answers.

The doctors often spoke of what she couldn’t or wouldn’t be able to do, and yet she has persevered through every step. Every step and accomplishment was worth celebrating, but the weight of caregiving is heavy. Eventually, I reached out to talk to a professional therapist. They explained that the grieving process, while challenging, was normal. All the anger, sadness, denial, and bargaining were leading to acceptance of the loss. The therapist explained that lost dreams needed to be grieved, too.

As I work toward acceptance and finding meaning, I’m often asked by others how I do it. My answer is: “I can’t say it gets better, but I can say you get better.” Accepting the loss is not the destination, but it is a part of the journey.

Nadia’s Story (Adulthood & Independence)

When all of this first happened, I worried a lot about the future for all of us. Would he accomplish his life’s goals? Would he go to college or get married? Now that he’s an adult, it’s so much better than I thought. It’s actually pretty normal. Some things are different though. He goes to college. We were really nervous sending him off, but he’s done great. He’s nonverbal, so he uses an AAC device that attaches to his power wheelchair. He has the typical teenager attitude. I wish when I was so worried I could have seen that it would all work out. It’s not what I imagined, but it’s still great.

DISCUSSION

The ability to actively listen to and to interpret the patient experience is vital to effectively address the needs of individuals within a particular community. TREND Community's proprietary artificial intelligence (AI) analytics engine, Krystie$_{TM}$, was used to capture the perspective and experiences shared online by caregivers of children affected by HIE.

In a novel partnership with Hope for HIE, a global organization dedicated to awareness, education, and support for neonatal and pediatric acquired HIE, TREND Community identified key MH and EW touchpoints along the HIE caregiver journey through an analysis of the real-world conversations taking place within online caregiver support groups. The real-world conversation data analyzed represented several thousand community voices and caregiver experiences spanning more than a decade.

We identified 6 key MH and EW touchpoints along the HIE caregiver journey:

- Birth or Event (eg, near drowning)
- Post-Event & Acute Care (eg, NICU)
- Transition Home
- Milestone Moments (eg, developmental milestones such as walking or birthdays) & Transitions of Care (eg, early intervention to kindergarten)
- Adulthood & Independence (a spectrum of experiences)
- Loss (eg, loss of hopes and dreams or death of loved one)

We then conducted a targeted analysis of the conversations at each touchpoint, documenting key themes/topics that emerged and the MH and EW language used.

ADDITIONAL RESEARCH

Although this exercise highlights the complexity of the caregiver journey, our research team proposes further analysis around the affect of 'joy' at the early stages and 'transition home' to inform a curriculum that enables MH professionals to deliver aligned and informed individual and peer support to the HIE community.

JOY

Positive aspects of caregiving are reported less often in the literature compared to the negative experiences.[13] Some positive feelings discussed are a sense of pride, satisfaction, and accomplishment in fulfilling one's caregiving responsibilities. Caregivers have also reported in surveys feeling a more profound understanding of self and more significant meaning in life than they felt before the birth/event.[7]

Our analysis of emotional language at early stages revealed that joy was expressed at all stages (pregnancy, birth, NICU, and discharge). A data exploration of these conversations might shed light on the specific experiences that elicit this emotion.

Transition Home

One unmet need of the HIE community is providing support for parents as they transition home after the post-event/acute care period (B. Pilon, personal oral communication, April 13, 2022). This stage can be filled with joy at going home, yet intense fear in realizing that they no longer have full support from hospital staff. In addition, navigating specialist appointments, therapies, other health services, early intervention requests, financial and insurance applications, job responsibilities, daycare for special needs infants, and care of siblings; finding peer-to-peer support; and facing other challenges are all-consuming changes in their lives.

Few studies have pursued this unmet need in rare and chronic disease communities. A data exploration of the real-world conversations happening at this touchpoint could fill this gap in the medical and scientific literature.

COMMUNITY LEXICON

Words have the power to heal, guide, and motivate. A data exploration aimed at understanding the community lexicon could help MH professionals understand how this community talks about MH issues and the emotional weights of specific terms and phrases.

EXPANDING THE CAREGIVER JOURNEY MAP

Based on the research that we have conducted across myriad rare diseases, we anticipate that the caregiver journey map will vary from community to community. For example, because of HIE's sudden onset, the diagnostic journey did not emerge as a key touchpoint. Expanding our research to other caregiver communities will lead to a more comprehensive (and complex) rare disease caregiver journey map. Identifying the commonalities in caregiver experiences across rare diseases could be used to expand the curriculum to enable MH professionals to deliver aligned and informed individual and peer support to rare caregivers more broadly. We propose the following conditions as topics for future phases of this research:

- Prader-Willi Syndrome
- Friedreich’s Ataxia
- SLC6A1

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APPENDIX

Hypoxic-Ischemic Encephalopathy Community Voice Report

Caregiver Journey Literature Review: Hypoxic-Ischemic Encephalopathy

Hypoxic Ischemic Encephalopathy

Community Voice Report

Prepared for Hope for HIE Support (Hypoxic Ischemic Encephalopathy) Parent Forum

Nervous System

TREND Community™
Turning Anecdotes Into Evidence™

Capturing Patient Experience Data

The Problem

Capturing patient experience data and applying it to the drug development and regulatory process is often lengthy, laborious, and expensive. This is further complicated for rare diseases where affected patient populations are typically small, heterogeneous, and widely dispersed.

The Solution

TREND analyzes years of real-world experience data shared within social networks to gain valuable insights into the community's perspective on living with rare disease. These data are de-identified and summarized into a Community Voice Report, which can then lead to Data Explorations and Health Initiatives.

Community Voice Report

The Community Voice Report follows the FDA's patient input Guidelines for Patient-Focused Drug Development meetings and aims to quantify disease burden, disease management strategies, and possible unmet needs.

Data Explorations

TREND Data Explorations further analyze existing social data to uncover deeper insights. Unlike the breadth of a Community Voice Report, Data Explorations examine a single topic and reanalyze the surrounding posts, comments, and feedback to better understand the community's interest.

Health Initiatives

TREND Community Health Initiatives bring community members together on the TREND Community™ platform to collectively track specific data and explore potential solutions to address an identified unmet need.

> ***"The TREND report was invaluable in helping us define the questions and multiple-choice answers that should be included in our Externally Led Patient Focused Drug Development Meeting last June."***
>
> *—Kyle Bryant, FARA, rideATAXIA Founder/ Program Director*

TREND Community categorizes diseases using the Genetic and Rare Diseases (GARD) Information Center database.

- Cancer
- Congenital\Genetic
- Viral Infections
- Musculoskeletal
- Skin Diseases
- Nervous System
- Metabolic
- Blood Diseases
- Endocrine

How It Works

All of our projects start with community engagement. Due to the unique difficulties of rare and chronic disease, many groups have created social networks online to support and validate each other. In these groups, community members are able to tell stories, promote advocacy, and share advice for managing symptoms, navigating the health care system, and living with a rare or chronic disease. We connect with individuals and leaders in these communities to learn about their illnesses, understand the current state of medical knowledge, and determine how our partnership can best address their unmet needs.

Once we have established a relationship with the community and gained consent, we download the deidentified data from these social media streams. These data are run through our analytics engine, named Krystie after the dear daughter of one of our community members. Krystie quickly analyzes vast amounts of data from years' worth of community discussion. Analysts manually code a sample of the data to validate the algorithms and train the engine to identify deeper insights (for example, to detect whether the speaker is a patient or a caregiver). This analysis culminates in a custom Community Voice Report.

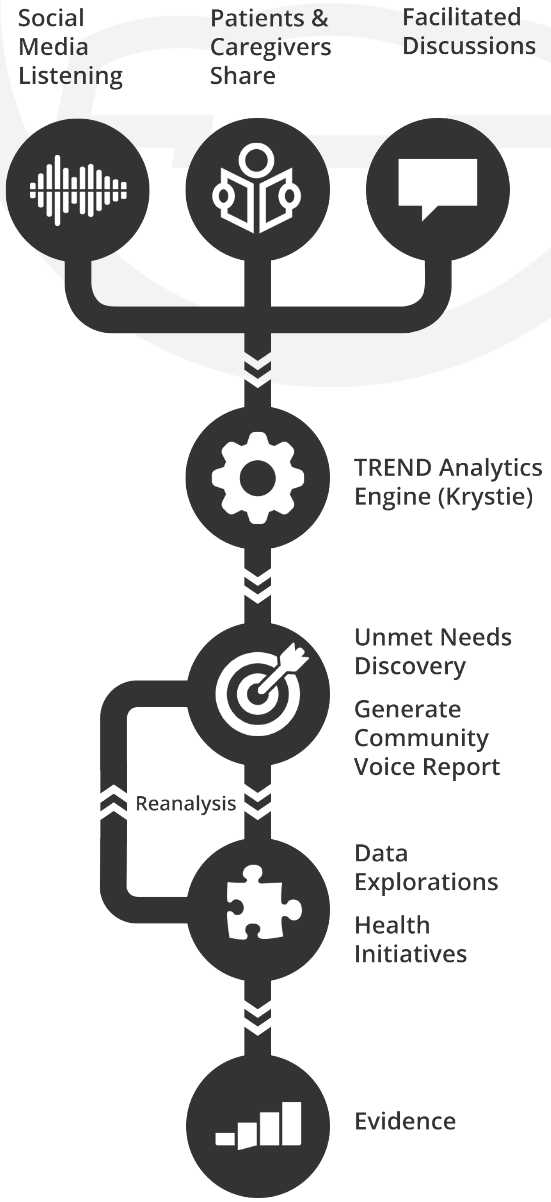
These Community Voice Reports are shared with the community free of charge, and our industry stakeholders have the opportunity to license the data for projects that address unmet needs and improve quality of life. These insights may be used to design Data Explorations or Health Initiatives.

Industry Stakeholders use TREND data to:

- Establish disease natural history
- Identify unmet therapeutic needs
- Understand quality of life issues
- Design better clinical trials
- Build a case for patient-centered regulatory approvals

Community Stakeholders use TREND data to:

- Inform medical and support teams
- Educate family members
- Catalyze research
- Spread awareness and advocacy



Overview

Hypoxic Ischemic Encephalopathy (HIE) is a neonatal brain injury caused by oxygen deprivation or reduced blood flow to the brain. HIE can occur before, during, or after the birth process, and can be caused by a variety of complications (including, but not limited to, umbilical cord complications, placental or uterine complications, blood clotting disorders, extremely low maternal blood pressure, trauma during delivery, cardiac arrest, or near SIDS events). There is a wide range of outcomes associated with HIE, including cerebral palsy and other neuromuscular issues, seizure disorders, difficulty breathing and swallowing, vision and hearing issues, gastrointestinal issues, and cognitive or developmental delays.[1] Prevalence estimates vary from 2 to 9 in every 1,000 live births.[2]

In 2011, the non-profit organization Hope for HIE created a private Facebook group for individuals and caregivers in the community to connect, share advice, and support one another. In May 2019, TREND analyzed and compiled this conversation data. The following report provides perspectives and insights on living with Hypoxic Ischemic Encephalopathy.

Facebook Group Stats

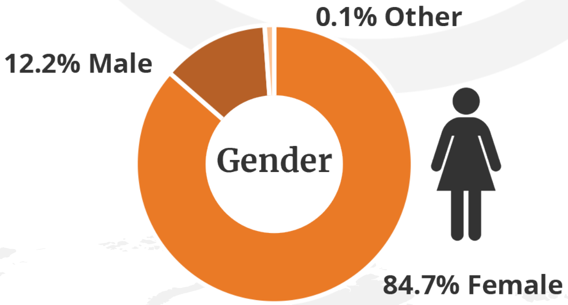
Hope for HIE Support Parent Forum

As a key component of the Hope for HIE foundation outreach networks, this is a private discussion group for parents, and approved immediate family members, of children diagnosed with Hypoxic Ischemic Encephalopathy (HIE).

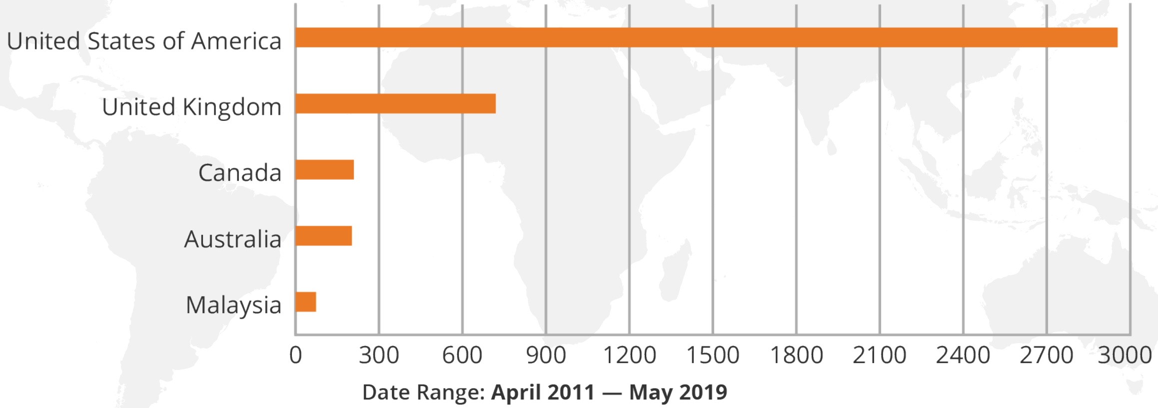
4,637
Members

43,213
Posts

513,659
Comments



45%
Ages 25-34



Date Range: **April 2011 — May 2019**

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Disease Burden

In this community, parents and caregivers express the symptoms and burdens of HIE through stories, questions, and discussions. From these conversations, we have identified the predominant disease burdens. The results of this analysis are illustrated on the right.

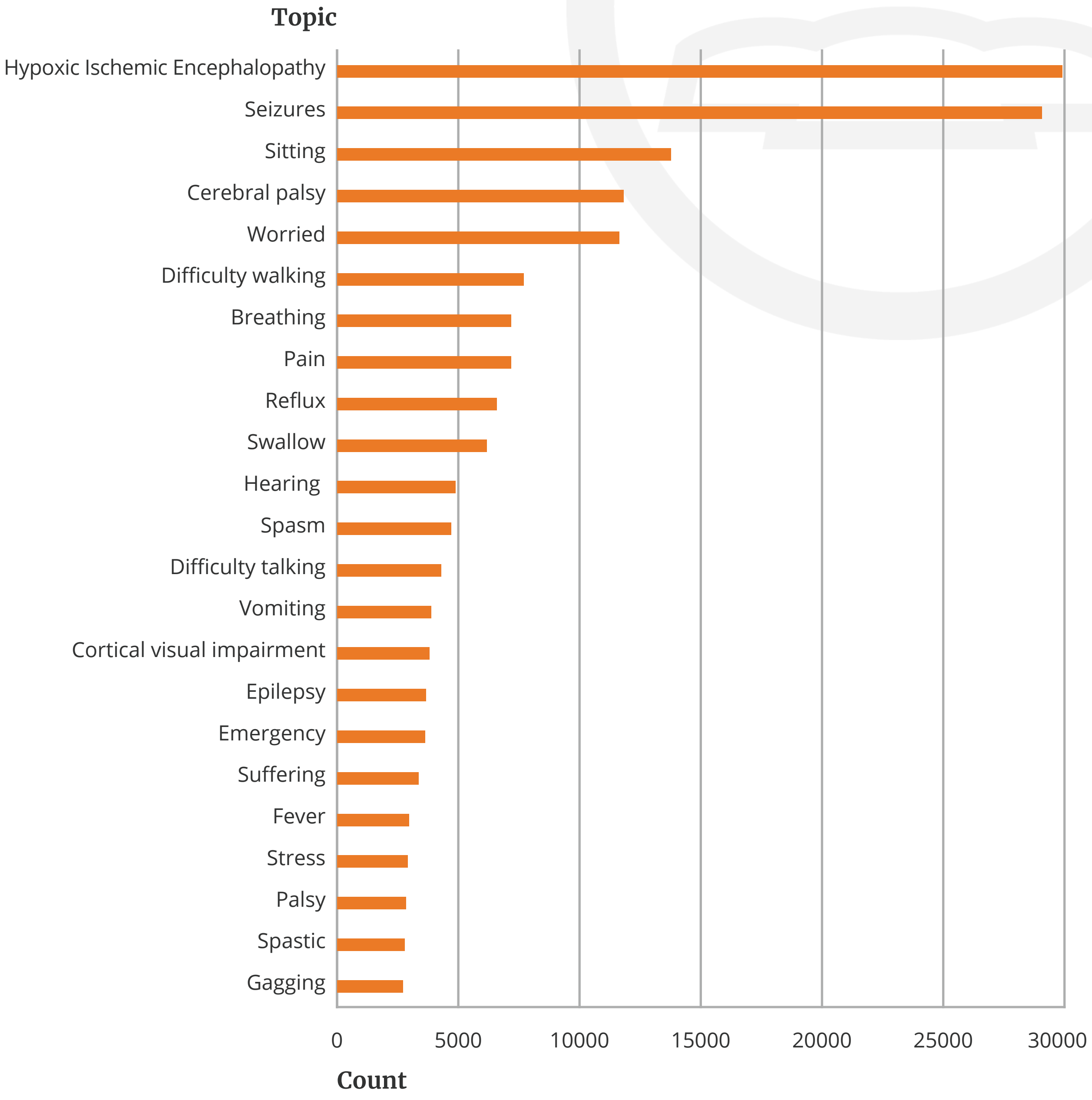
Given the range of outcomes and symptoms associated with HIE, we have identified five major categories of burden.

These include:

- Seizures and Epilepsy: 32,735
- Mobility: 32,229
- Breathing and Swallowing: 18,558
- Worry and Anxiety: 14,205
- Gastrointestinal issues: 10,464

"I worry the most about how my son will make his way in the world. Between physical challenges, significant speech challenges, and then society making assumptions about his intelligence and capabilities, he's got a lot of obstacles to overcome."

—Community Member

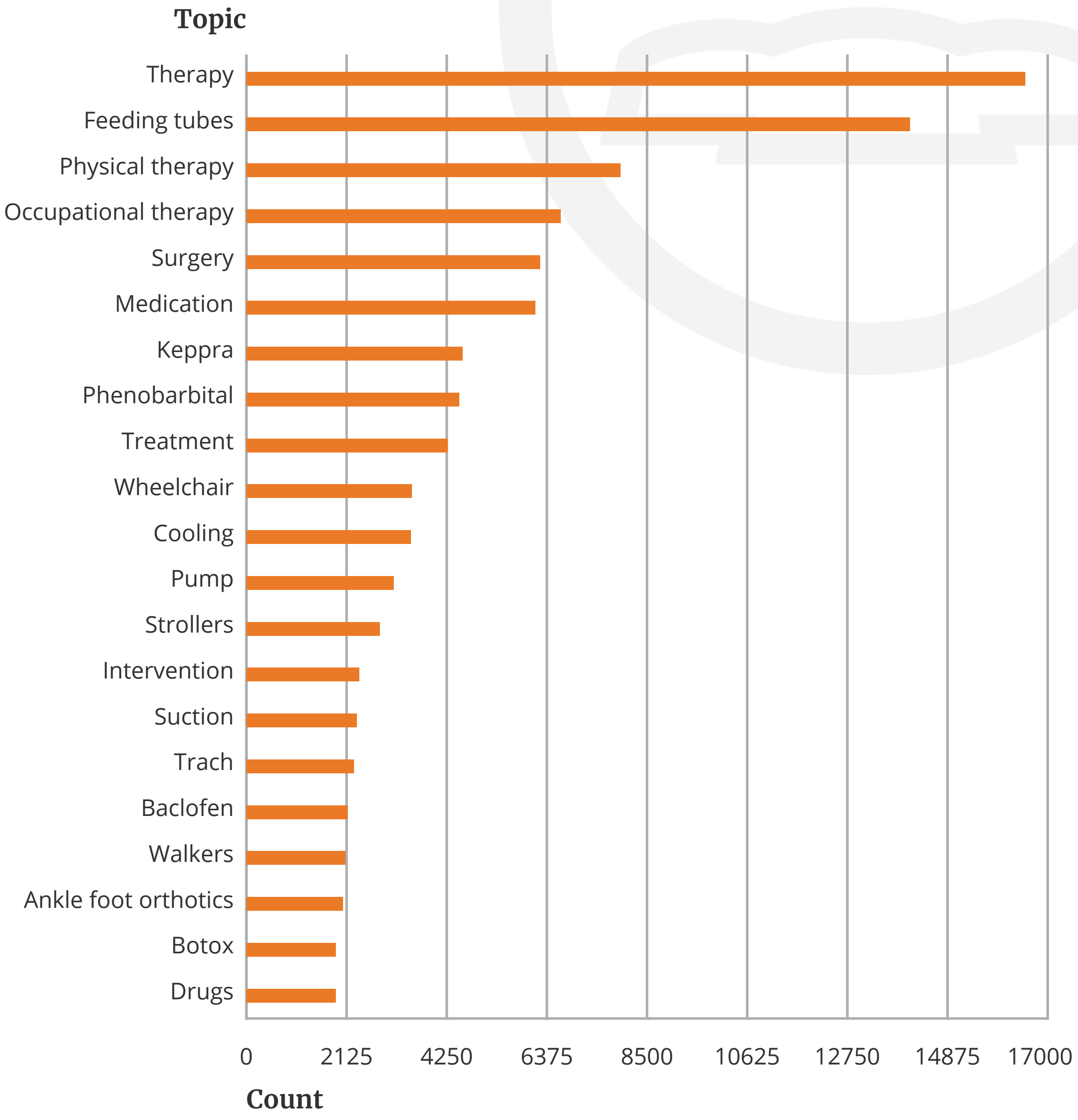


Disease Management

As there is no cure or specific treatment for Hypoxic Ischemic Encephalopathy, caregivers employ a combination of management strategies. Advice and anecdotes about these methods are a major topic of conversation in the community. The results of our disease management analysis are illustrated on the right.

Therapy (16526) is the most frequently mentioned treatment strategy. Common therapies include *physical therapy* (7937) and *occupational therapy* (6666). These conversations often include commentary on the importance of early intervention therapies, difficulty finding and paying for therapies, and other related issues.

Cooling (3489), also known as therapeutic hypothermia, is one of the most important treatments for HIE, and has been proven to reduce outcomes of mortality or major neodevelopmental disability.[3] These conversations often include comments about individual experience with cooling or discussion of recent medical research on the subject.



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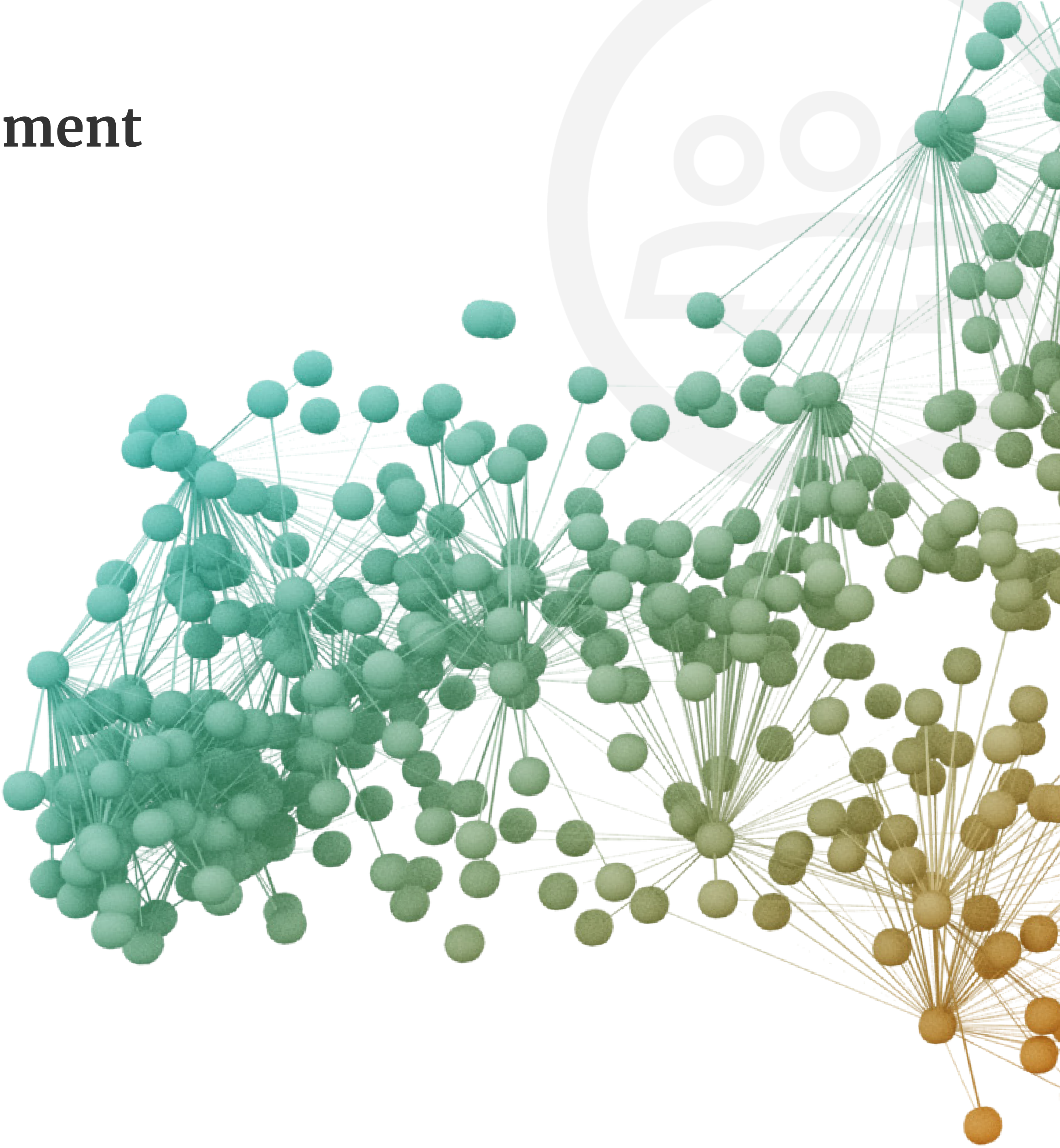
Disease Management

Feeding tubes (14073) also appear regularly in the community conversations. Feeding tubes can be used to address both gastrointestinal issues and difficulty breathing and swallowing.

General terms related to *medication* (6122) and *drugs* (1891) appear 8,013 times. Community members specifically mention *Keppra* (4588) and *Phenobarbital* (4517), which are used to treat seizure disorders, and *Baclofen* (2144), which is used to treat muscle symptoms such as spasms, pain, and stiffness.



"When we found other parents going through the same thing as our child was in the NICU, I felt hope for the first time. Even though we didn't know if our child was going to live or die, not being alone made all the difference in the world. As my son grew, it helped me find a courage I didn't know I had inside me and empowered me to advocate for his needs."

—Community Member

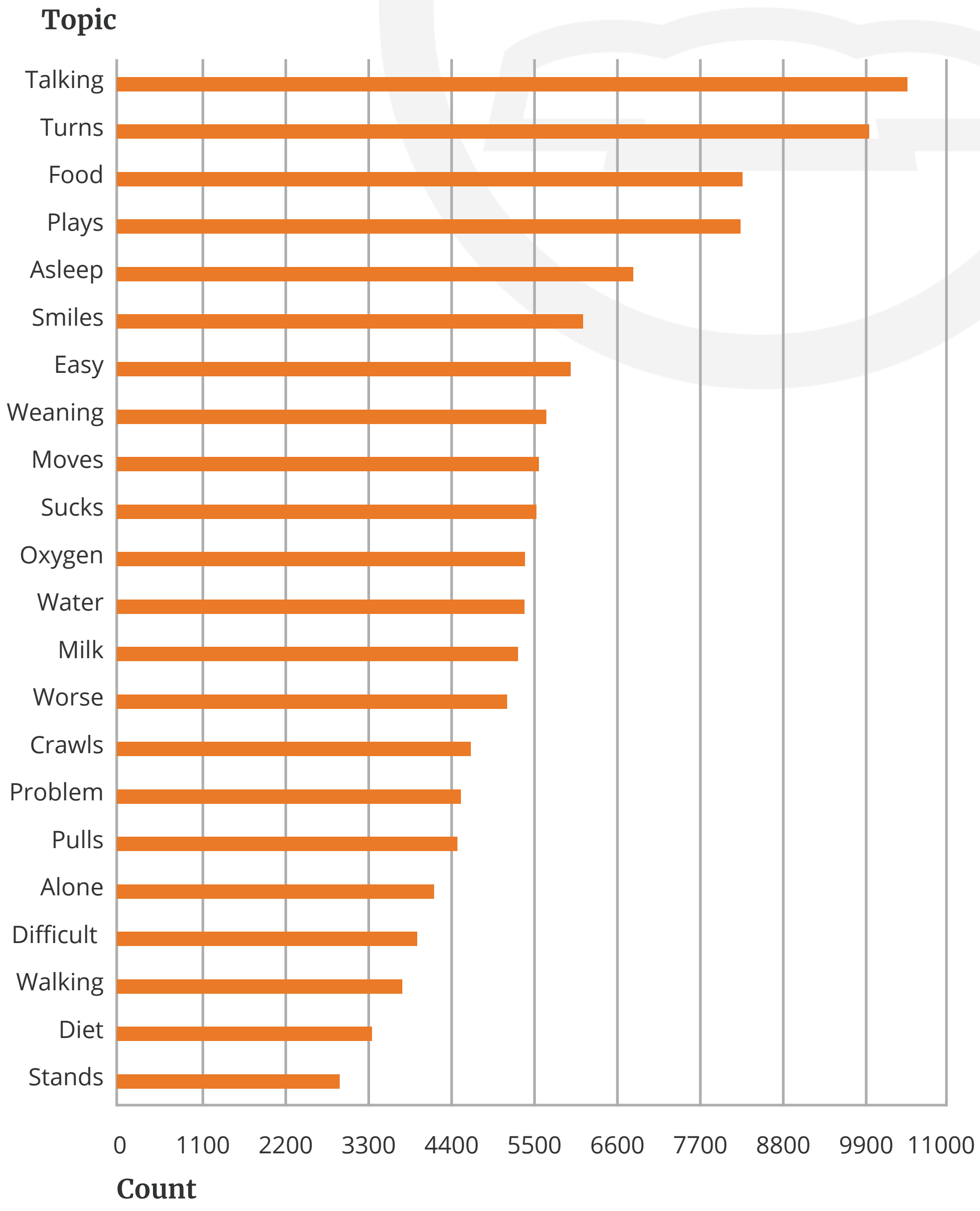
Significant Terms

The graph on the right illustrates significant terms that appear throughout community conversations. The frequent use of these terms indicates their importance; however, they require further investigation to determine how they relate to the symptoms and management of Hypoxic Ischemic Encephalopathy.

Terms related to *talking* and *speech* appear 10,490 times in the community conversations. While some of these comments refer to conversations with care providers and community members, others highlight speech as a major developmental hurdle for children with HIE. Caregivers share stories and updates about verbal abilities and discuss various therapies and alternative communication strategies.

Like speech, many individuals with HIE experience different degrees of mobility. Terms related to movement, such as *plays* (8273), *moves* (5596), *crawls* (4696), *walking* (3788), and *stands* (2955), are mentioned regularly.

Given the prevalence of eating and gastrointestinal issues, conversations related to diet and nutrition figure heavily into the community conversations. *Food* (8298), *milk* (5320), and *diet* (3382) all appear frequently.



Discovering Unmet Needs

Our conversation analysis indicates several areas of unmet need in the HIE community. Community members regularly express the need for further medical research, education, and awareness to support existing patients and prevent further incidents from occurring. These conversations highlight several key areas of interest, including, but not limited to, hypothermia therapy or cooling, early intervention therapies, accurate assessment, and understanding the initial injury.

As mentioned in the disease management section of this report, cooling or therapeutic hypothermia is an important treatment development for individuals and caregivers impacted by HIE. Cooling is now considered a standard of care for eligible infants; however, not all hospitals are properly equipped, which is problematic because cooling is considered most effective within the first six hours. Community members highlight the need for further research to continue improving care standards and better understand the long-term efficacy of therapeutic hypothermia.

Similarly, community members regularly emphasize the importance of early intervention therapies. Therapy is the most frequently discussed treatment strategy in this community, and many individuals share questions and advice about different therapeutic practices. Recent research indicates that, due to neuroplasticity, various early intervention therapies can dramatically improve developmental outcomes. Many individuals stress the importance of improving research and education on this topic, especially given the emotional upheaval and uncertainty of the first few years with HIE.

Many caregivers mention their desire to better understand the circumstances surrounding the initial brain injury. A few also mentioned having *post-traumatic stress disorder* (696 mentions) or similar emotional responses to the trauma of the birth and moment of injury. Discussing and interpreting what happened within the safety of the group seems to be an important way of processing and gaining acceptance of the events and outcomes.

Data Explorations and Health Initiatives

This Community Voice Report is the first step in understanding the research implications of the conversations happening on social media about living with Hypoxic Ischemic Encephalopathy. Using these findings as a starting point, TREND Community can continue to work with this data and the HIE community to determine priorities for further research.

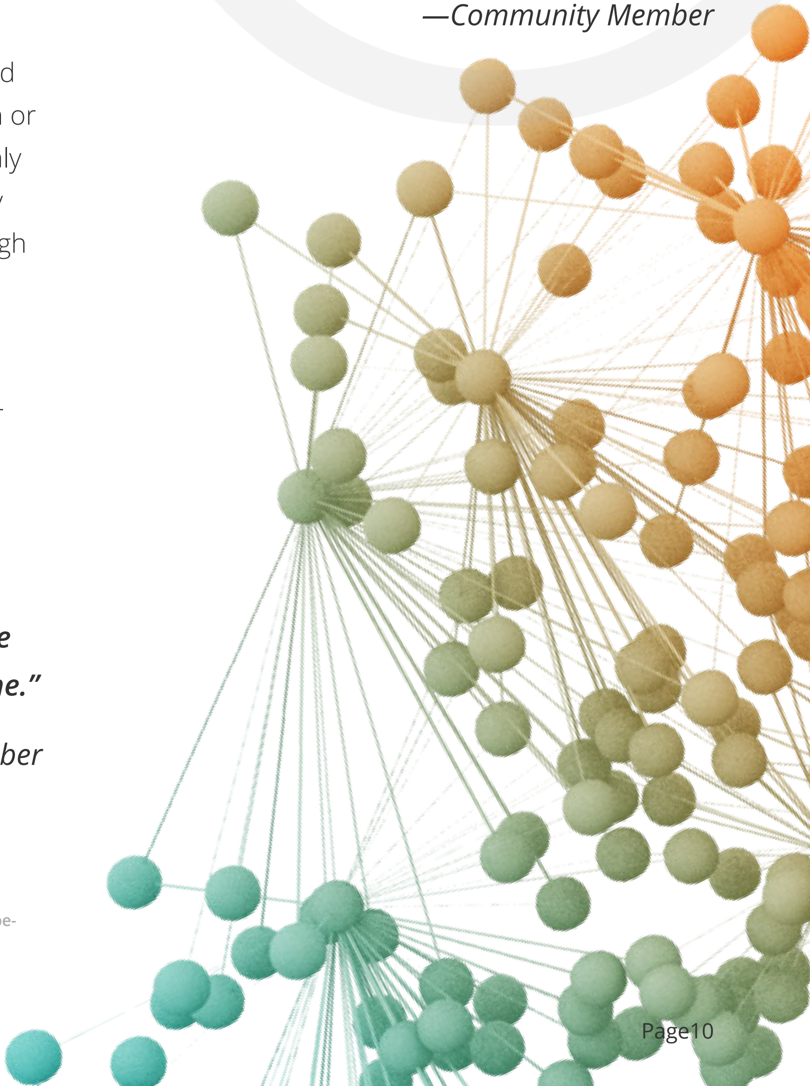
Building on the breadth of this report, a Data Exploration can examine the existing conversation data to better understand significant topics and areas of interest. Using this evidence, a Health Initiative could then be designed to address the community's specific needs and accelerate research. We have detailed a few possibilities below.

Given the interest and importance of early intervention therapy, we recommend an initial Data Exploration to better understand the conversations about this topic. In addition to expressing their interest in early intervention research, community members regularly share anecdotal reports about the effectiveness of various therapies in the months and years after their child's initial injury. By conducting a thorough examination of the existing conversation data, we could identify the common intervention strategies and how they correlate to the injury, severity, and outcomes.

The conversations also highlight a desire for better understanding and assessment of the potential outcomes associated with HIE. Despite the vast array of symptoms associated with HIE, the current diagnostic tool, the Sarnat Scale, only offers three classifications of severity and is based on how the baby appears after birth or injury.[4] Considering that the impact of HIE only becomes apparent as a child develops, many caregivers express interest in a more thorough assessment strategy. A Data Exploration or Health Initiative could be designed to investigate these trends and inform the development of assessment tools that better inform the community needs.

> ***"With every HIE being different, I don't know how it will affect my child's life. We just have to take things one day at a time."***
>
> *—Community Member*

> ***"HIE results in a huge variable of outcomes. No two injuries are alike and therefore no two outcomes will be alike. But each and every life is valuable, regardless of outcome."***
>
> *—Community Member*



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4 What is HIE? (n.d.). Retrieved June 28, 2019, from https://www.hopeforhie.org/whatishie

Data Explorations and Health Initiatives

Developmental challenges related to speech and mobility are a significant topic of interest in this community. A Data Exploration could be designed to analyze the commonalities and differences among these experiences and track the efficacy of various treatment strategies, including therapies, operative procedures, medical devices, and medications.

Given the range of outcomes, many of the symptoms highlighted in our disease burden analysis invite further investigation. Data Explorations or Health Initiatives could be designed to specifically analyze the community conversations surrounding seizure disorders, breathing difficulties, and other major areas of concern.

Finally, we recommend a Data Exploration to investigate the high reports of emotional and psychological distress, including *worried* (11642), *stress* (2907), *anxiety* (2563), *irritable mood* (1745), *emotional* (1386), *post-traumatic stress disorder (PTSD)* (696), and *depression* (510). This research could explore the lasting impact and trauma of the birth or initial injury on both patients and caregivers. Building on this evidence, a Health Initiative could be designed to monitor these symptoms and experiences over time. These projects have the potential to inspire awareness, education, and support for this unmet need.

Like this report, future Data Explorations and Health Initiatives could be used to better educate medical professionals and address these unmet needs. Through this partnership, TREND Community hopes to accelerate these findings and improve the quality of life for individuals and caregivers living with Hypoxic Ischemic Encephalopathy.

> ***"Being able to connect with other parents who understand the daily life we live is just invaluable. It helped me find the strength to not only survive but to thrive. It helped me become an advocate. It helped me become a better me."***
>
> *—Community Member*

About TREND Community

Founders

TREND Community™ was founded by the parents of a child with Prader-Willi Syndrome who understand the needs of the rare and chronic disease community.

Our mission is to improve the quality of life for everyone living with rare and chronic disease.

Security

TREND secures all social data with state-of-the-art, private cloud servers. Our security practices comply with current HIPAA, FDA, and GDPR guidelines.

Disclaimer

The researchers who prepared this report are not doctors, are not providing medical advice, and are only reporting what was said in the online conversations.

IRB Exemption Status

Western Institutional Review Board determined that this study is exempt under 45 CFR § 46.104(d)(4), because the aim of the research is to collect de-identified information from social media posts to better understand disease burden, disease management strategies, quality of life, and the unmet needs of patient communities living with rare and chronic diseases. The research is not FDA-regulated nor classified, does not involve prisoners, and is consistent with the ethical principles of the Belmont Report.

Quotes

All quotes were provided by consenting community participants through one-on-one interviews or online focus groups conducted on the TREND Community™ platform. Names are not included to protect participant privacy.

Data Ownership

Ownership of public posts or conversations from other social media platforms shared with TREND for analysis are subject to the social media platform's privacy policy, terms of service and other applicable policies. Participants who share data and experiences on the TREND Community™ platform give their consent for TREND to analyze it. TREND Community owns the results of our analysis and all other data and output that we produce including our Community Voice Reports.

License

TREND Community™
Turning Anecdotes Into Evidence™

Caregiver Journey Literature Review

Hypoxic-Ischemic Encephalopathy

INTRODUCTION

Caregivers of patients with hypoxic-ischemic encephalopathy (HIE) undergo high levels of acute stress at the time of the birth/event and during the post-event/acute care period. In most cases, the event unexpectedly occurs at birth, leaving parents filled with shock, fear, anguish, anger, disbelief, and devastation, and putting them at substantial risk for post-traumatic stress disorder (PTSD).[1-4] During the birth/event and post-event/acute care period, parents who are now caregivers to their injured infant or child are especially vulnerable; clinicians and nonclinical staff must consider an empathetic and measured approach to prevent additional traumatization and retraumatization of the caregivers. Mental health professionals are uniquely positioned to train hospital staff and physicians on techniques to mitigate further trauma during hospitalization and to support these parents as they transition home.

Keywords: caregiver journey, caregiver burden, stressors, role strains, intrapsychic strains, hypoxic-ischemic encephalopathy (HIE), anxiety, transition of care, hypothermic therapy, NICU, cerebral palsy, epileptic seizures, post-traumatic stress disorder (PTSD)

METHODS

The search engines and databases used to access articles included MEDLINE, PubMed, APA PsycArticles, APA PsycNet, EBSCO, Google Scholar, and CORE Open Access, with an emphasis on retrieving academic peer-reviewed publications. DOAJ was used to verify open-access journals. The search focused on the literature associated with background information related to categories of stressors affecting caregivers related to chronic disease, rare disease, and HIE in particular. Mitigation strategies related to caregiver burden were also explored in the literature.

RESULTS

In this review, articles were selected based on their relevance to the HIE caregiver journey. Caregiver burden models were explored, with an emphasis placed on those related to chronic disease, rare disease, and more specifically, HIE. Background information on HIE was included to provide context on how the associated severity of symptoms and intensity of treatments impact the caregiver differently based on their unique experiences. Last, information on mitigation techniques, trauma-informed care, family-centered models, and assessments to identify caregiver burden was reviewed to shed light on how these measures may be incorporated into the HIE community.

DISCUSSION

BACKGROUND ON HIE

Hypoxic-ischemic encephalopathy (HIE) occurs in approximately 2 to 3 out of 1000 live births[5-7] and up to 26 out of 1000 births in developing countries.[8] The event leading to HIE usually occurs at or around the time of delivery. It results from low oxygen levels and inadequate blood flow to the brain and other organs; this leaves the infant with brain injury from the reduced cardiac output and, subsequently, reduced blood flow to the cerebral cortex, with associated oxidative stress and inflammation.[8-10] Even if the neonate overcomes respiratory acidosis, metabolic acidosis leaves the infant vulnerable and unable to recover, resulting in permanent injury.[11]

Neonates with HIE often present with hypotonia, decreased responsiveness to stimuli, impaired mental status, altered reflexes, and respiratory difficulties.[12] Possible causes of and risk factors for HIE from perinatal asphyxia range from placental abruption to umbilical cord issues, maternal cardiovascular collapse, fetal loss of blood, meconium aspiration, uterine rupture, and unknown factors.[13] In light of new understandings of placental and umbilical cord abnormalities,[14] metabolic disorders, and genetic disorders as causes of neonatal encephalopathy (NE), considerations must be taken to evaluate all contributing factors before arriving at a diagnosis of HIE.[15] It has been suggested that the cause of HIE is unpredictable and that unless a specific sentinel event is identified, it must be proposed that the neurological injury might have occurred in the fetus before labor even began.[16] It is worth noting that a sentinel event is identified in only a small percentage (15%-29%) of cases of HIE.[11,17,18]

Specific diagnostic criteria must be met to make a diagnosis of HIE. A comprehensive etiologic exam must be performed to rule out other causes for presenting symptoms, or a diagnosis of NE must be made instead of HIE. The criteria to consider for making a diagnosis of HIE at birth are the following: Apgar score of less than 5 at 5 minutes and 10 minutes, abnormal Sarnat examination,[19] low umbilical cord arterial gas pH levels, neuroimaging evidence on brain imaging studies consistent with a hypoxic-ischemic event, multisystem organ failure consistent with HIE, a sentinel hypoxic-ischemic event immediately before or during labor and delivery, fetal heart rate patterns consistent with an acute peripartum or intrapartum event, and no evidence of other underlying factors that may contribute to pathogenesis.[12,13,20]

Karamian et al[12] summarized the following diagnostic features that distinguish HIE from other causes of neonatal brain injury not linked to direct hypoxic-ischemic events: genetic factors, ischemic strokes, neuromuscular disorders, brain or other central nervous system disorders, infection, environmental toxins, malformations associated with hereditary factors such as congenital heart disease, inborn errors of metabolism, NE secondary to brain malformations, and rare metabolic disorders. Other causes involve vascular and thrombolytic conditions—that is, arterial ischemic stroke and cerebral venous thrombosis—which have many etiologies associated with genetic factors that were not previously appreciated in the clinical setting.[11,12,20,21]

Identifying antepartum and intrapartum risk factors for HIE has been a challenge, with much speculation as to which determinants and interventions show statistical significance in study results. In a meta-analysis by Rossi and Prefumo,[16] risk factors associated with an infant later being diagnosed with HIE included intrauterine growth restriction (IUGR), labor augmentation, emergency cesarean section, nonreassuring cartography (CTG) results on monitoring fetal heart rate, detection of meconium, and chorioamnionitis. It is possible that neonates with IUGR were not in a position to tolerate labor well because of other circumstances. All other risk factors—male sex, nulliparity, maternal smoking, maternal hypertension, labor induction, gestational diabetes, polyhydramnios, and vacuum extraction—fell under limits that were not significantly different from those of controls, even though there have been inquiries into whether these are contributing factors to increased risk for HIE.[16]

Management for neonates with HIE includes supportive care to restore blood flow to the brain, respiratory support, and the introduction of medications to treat seizure activity. With the advent of hypothermic therapy within 6 hours of birth, there have significant improvements for both mortality and disability outcomes, with subsequent studies showing benefits from cooling therapy for up to 24 hours postbirth; selective head cooling and whole-body hypothermia have been used, depending on the situational needs.[9,22-25] The Sarnat Score system[19] was developed 46 years ago to evaluate abnormal neurological presentation in infants and still forms the framework for identifying when therapeutic hypothermia would be an appropriate treatment after birth or a hypoxic-ischemic event; modifications to the scoring system have been made to keep in step with updated research findings.[26,27] Four meta-analysis trials with hypothermic cooling showed consistent efficacy as well as a marked improvement in infant outcomes for both mortality and disability.[23,28-30]

In addition to hypothermic therapy, treatment options are focusing on administering neuroprotective agents. These are used to clear free radicals and reduce inflammation, thereby preventing further cell damage. Agents being studied for this purpose include melatonin, allopurinol, magnesium sulfate, erythropoietin (EPO), *N*-acetylcysteine (NAC), topiramate, xenon, and stem cells.[10]

Comorbidities resulting from HIE include cerebral palsy (CP), epilepsy, secondary microcephaly, gastrointestinal disorders, learning and attention issues, autism-related behavioral challenges, hearing issues, and vision problems, as identified by hopeforhie.org.[31] It is relevant to explore when these comorbidities begin for the patient to understand their impact on the caregiver. Hearing and vision changes, secondary microencephaly, and CP are usually diagnosed within the first 2 years of life, with CP resulting from HIE occurring in 10% to 15% of all CP cases. Epilepsy in HIE can occur immediately following the traumatic event, or it can begin at any stage later in the journey. It most often follows a pattern of starting at ages 4, 6, and 8 years and during puberty, as these represent critical developmental times in brain growth. These 'wait-and-see' periods can be very stressful for parents (B. Pilon, personal oral communication, April 13, 2022). In addition, learning and attention issues, behavioral changes, and autism are diagnosed from 18 months to upwards of the preteen and teenage years.[8,31-34]

Less common than occurrence at birth is HIE acquired in childhood, resulting from near miss sudden infant death syndrome (SIDS), near drowning, near suffocation, or other trauma that leads to prolonged resuscitation efforts with resultant brain injury.[35] Patients in these cases are transferred to the pediatric intensive care unit (PICU) for post-event acute care. Diagnostic measures and management strategies for children with HIE secondary to trauma include brain magnetic resonance imaging (MRI), complete blood count, echocardiogram, and follow-up with hematologists. Treatment options in the acute phase are similar to those discussed above for neonates: supportive care, treatment of seizure activity, and hypothermia therapy.[35]

CAREGIVER STRESSORS AND BURDEN

Typically, the role of the caregiver has been defined as a person who is "informally" caring for the needs of the care recipient by not accepting financial compensation. Often, this job is assumed by family members who find themselves in a dual role of medical advisor and caretaker for both the physical and emotional aspects of the recipient's care. Over time, this can unduly stress the caretaker, especially if there is no balance between the care responsibilities and self-care or if it is expected that the caretaker assumes their role in a 24 hours/7 days per week capacity.[36,37] Adelman et al[38] noted that there is no *International Classification of Diseases* (*ICD-9* or *ICD-10*) code for caregiver burden even though it can cause significant disruption and emotional trauma to the caregiver. Zarit et al[39] defined caregiver burden as "the extent to which caregivers perceive that caregiving has had an adverse effect on their emotional, social, financial, physical, and spiritual functioning." Bastawrous[37] proposed that "caregiver burden" should be better studied and defined by mixed-methods approaches rather than exclusively quantitative measures. The contextual aspect of caregiver answers on traditional assessment methods is often lost and does not consider the holistic patient experience.

STRESS THEORY

A model of stress theory was proposed by Pearlin[36] when evaluating the stressors and burden in caregivers of aging patients who were no longer able to care for themselves at home without assistance, with concepts applicable to caregivers of many patients with chronic illnesses and rare diseases. Pearlin proposed a model of stress theory that categorized stressors and caregiver burden into primary stressors and secondary stressors. Stressors are factors that elicit cognitive, behavioral, or emotional reactions in the caregiver, often used in a negative context regarding caregiver experiences.[38]

Primary stressors are strains that affect the caregiver resulting from direct care of the recipient and involve a wide range of aspects of care—that is, medical, financial, legal, and logistical supports. Activities of daily living (ADLs) consist of bathing, transferring, dressing, toileting, grooming, feeding, and administering medications to the patient. Instrumental activities of daily living (IADLs) involve logistical activities for the patient: transporting the patient to and from appointments, managing finances, preparing meals, and giving emotional support. IADLs include a wide range of aspects of care, such as medical, financial, legal, and logistical support.[40]

Secondary stressors come from outside the direct activities of caregiving. They comprise *role strains* that affect other aspects of the caregiver's life as a result of performing all the ADLs and IADLs: interaction with spouses and partners, other children in the household, relatives, friends, and coworkers; financial hardships; loss of time from their job; social exclusion; and cultural acceptance. *Intrapsychic* strains arise from within the caregiver and are associated with "diminishment" of self-concepts: low self-esteem, isolating behaviors, loss of normalcy, loss of social status, and loss of interest in activities that were once enjoyed; these can lead to depression and anxiety, sometimes manifesting with physical illness. All the stressors in the caregiver's life increase burden, and if not mitigated with support strategies, they can lead to adverse mental and physical health outcomes.[36,38]

Yates et al[41] went on to explore incorporating an appraisal model[42,43] with Pearlin's stress model to understand how a caregiver's perception of their stressors relates to their sense of satisfaction in their position. Two caregivers with an equivalent stressor may respond quite differently to the same strain and burden,[37] so this approach will clarify the holistic aspects of the caregiver's experience.

ROLE THEORY

The model of role theory explains how a person defines their status and social position in society and how their subsequent behavior is based on that role. Biddle[44] expanded on Goode's[45] theory of role strain as related to caregiver burden. "Role overload" was explained as being the function of how the caregiver perceives their role and expectations. Overload only results when roles and expectations are out of balance, such as when there is not enough time or resources for the caregiver to fulfill their role. How the caregiver perceives that their role fits into their previous life and what pressures result from that perception enables them to feel satisfied or unsatisfied in their position, which then becomes part of their identity in society.

Adelman et al[38] felt that mixed-methods assessments, using aspects of stress theory with role theory, could better serve in understanding the holistic caregiver experience. Through systematic reviews and meta-analyses, it was proposed that these strategies be applied to assess caregiver burden by looking at individual stressors with the patient's perception of how they are affected by the strains. By understanding context, such as cultural awareness, gender issues, filial piety, and socioeconomic factors, measures could then be put into place to offer support strategies for the caregiver.[38]

Receiving less attention in the literature are the positive aspects of caregiving.[46] Some positive feelings reported are a sense of pride, satisfaction, and accomplishment in fulfilling one's caregiving responsibilities. Feeling a more profound understanding of self and more significant meaning in life than they felt before the birth/event have also been reported in caregiver surveys.[38]

CAREGIVER QUALITY OF LIFE

It is estimated that rare disease affects up to 30 million individuals in Europe and 25 million individuals in North America.[47-51] Even though this number represents a diffuse number in the overall population, its impact on society can be quite significant as the costs associated with healthcare services increase and resources decrease for caregivers.[51] With the advent of medical advances in recent years, the survival rates of pediatric patients with complex medical conditions have gone up dramatically, resulting in an increase in the number of caregivers who are navigating the healthcare system.[52-55] Quality of life (QoL) for the caregiver is typically compromised with depleted resources, and psychosocial factors play a larger role in caregiver outcomes, as noted on various assessment scales for depression and anxiety.[55-58]

Given that these caregivers are coming into regular contact with the medical community, one might reason that strategies would be implemented for healthcare workers to check in on how caregivers are doing emotionally and physically during the care recipient's appointments, especially because it has been shown that caregiver outcomes are directly linked to better patient outcomes.[59-61] However, it seems that caregivers have become the "invisible patient,"[38] with medical staff focusing on the needs of the patient, in part because of a lack of resources and education, thus failing to ask the caregiver pertinent questions related to how they are coping in the process.[38,62,63] It has been documented that if preventive and interventive measures are not taken, the health outcomes of the caregiver can suffer, resulting in harmful effects such as depression, anxiety, grief, hopelessness, loneliness, fatigue, disrupted sleep, weight fluctuations, depression and anxiety, post-traumatic stress disorder (PTSD), physical injury, physical decline, and cardiovascular disorders.[3,37,54,64-68]

In a study[69] of children with chronic illness and their caregivers, parents reported that they did not feel they had enough time for other siblings because of all the responsibilities and demands in caring for their child with the illness. Some parents in the study said the experience had brought them closer to their partner; however, most respondents admitted that the majority of the time, the burden of caregiving had negative consequences on their relationship with their spouse, with caregiving responsibilities taking up most of their time. An added stress was that many parents reported meeting with health professionals who did not have a firm grasp on their child's condition, which left parents feeling that they had to do the most of the investigation needed to obtain the best care for their child.[69]

Risk factors in the literature for caregiver burden include female sex, low educational attainment, residence with the care recipient, a high number of hours spent caregiving, experiencing depression, social isolation, and financial stress.[59] Another consideration is how accepting of care the recipient is, with more stress and burden placed on the caretaker when the recipient does not view them favorably and embrace them in that role.[36] If the patient's emotional and behavioral challenges are underdiagnosed and left untreated, this could potentially harm the caregiver and increase their burden; hence, if strategies are not put in place to prevent or intervene in alleviating stressors and burden, the caregiver's mental and physical health can suffer.[36-38]

Why some caregivers seem to fare better than others is not well understood. It appears that several variables need to be considered, such as care recipient behavior, the extent of caregiving demands, psychosocial stress, family dynamics, level of satisfaction in the role, and filial piety, with "care recipient behavior being the single most significant variable that predicts the caregiver's overall well-being."[70] It was suggested in a study on caregivers of patients with CP[70] that providing support and education to address the care recipient's behaviors may significantly impact the caregiver QoL and lessen caregiver burden. Studies using the Hospital Anxiety and Depression Assessment Scale (HADS)[71] in caregivers of children with chronic illness reported that psychosocial support had the most significant impact on parental mental health outcomes. Considerations that may also mitigate some of the adverse effects of caregiver burden are high self-esteem, higher education level, and having/using coping strategies. Factors that were less important in determining parental outcomes were the level of disability or cognitive functioning in the child.[54,71]

INTERVENTION STRATEGIES

In a study of 57 caregivers of someone with a rare disease, all respondents reported a negative impact of caregiving on their mental health, even though 50% maintained that they were in 1 or more support groups. Some of the comments made by respondents were "exhausting while mentally and physically draining," "we all feel lost or helpless sometimes," "suffocating at times," and "it's very stressful and causes anxiety."[40] In a review of the literature, Smith et al[72] noted a study that information to caregivers about the availability of support groups and specialist networks was delivered by chance rather than being provided as an integral part of the course of care.

Some discussion catalysts during visits with healthcare providers on the recipient's medical team for engaging caregivers are inquiring: how the caregiver is feeling health-wise and emotionally; whether they are taking care of themselves with regular physical exams; inquiring about their QoL; whether they have adequate support systems in place or available to them; and whether they have made emergency arrangements for the care recipient in the event of their illness or absence.[38] Other strategies may include ensuring that the caregiver feels they are part of the patient's care team, is practicing self-care to maintain their own health, has access to informational material regarding the patient's condition, and is making use of technology so the care recipient can remain as independent as possible.

Professionals should provide the caregiver with information on in-home care services and respite care if available in their situation.[38,73] Even if the caregiver burden remains the same, the implementation of small changes in "psychoeducation interventions, therapeutic counseling, [and] skills training" may help alleviate some of the caregiver's mood-related symptoms.[74] Additional follow-up assessments on caregiver outcomes with mixed-methods approaches will help assess how these measures are working for the caregiver.[37,75] Pediatric psychologists already working with the care recipient are positioned to help caregivers change the outcomes of caregiver burden; they can identify those struggling with stress and strains and assist them with finding resources for peer-to-peer support, financial agencies, and counseling services to alleviate some of their mental health struggles.[61]

FAMILY-CENTERED MODELS

Caregivers of children with chronic illness reported significantly lower QoL than did parents of healthy schoolchildren, Hatzmann et al[55] proposed a family-centered approach to support caregivers of children with chronic illness. The caregiver recipient and their siblings are negatively affected if the caregiver's health-related QoL and overall QoL are lower than what is typically reported.[76] Various intervention needs were identified in a study completed by Pelentsov et al.[69] Parents reported "feeling boxed-in outside the box," that is, feeling socially isolated and needing to speak to other parents of children with a similar rare disease and limitations for employment. Some reported frustration over "practicalities of care," or parents' perceptions that healthcare professionals are letting them down and not keeping up to date on the standards of care and healthcare needs for their child's situation, leaving the parents to be "the expert" on their child. Also, they reported difficulty navigating "relationships" outside the dyad (caregiver and recipient), that is, the impacts on partner relationships and siblings. It has been proposed that caregivers could benefit if medical professionals take the time to listen to parents and ensure they are receiving the necessary contacts for support services, including being more aware of their social, financial, and emotional needs so they can better care for the patient while understanding the caregiver's perspectives.

One area of immense trauma for caregivers is the neonatal intensive care unit (NICU) experience, which is filled with numerous, unfamiliar clinicians, staff, and medical interventions. Separating the infant from parents increases parental psychological distress and interferes with parent-child bonding opportunities. With survival rates of preterm infants increasing, there has been more attention to incorporating a family-centered approach to care in the NICU. Approaches that have been suggested are involving parents in the care of the infant, allowing as many skin-to-skin bonding opportunities as possible (eg, "kangaroo care"), and promoting caregiver opportunities, parental empowerment, and shared decision-making during the care of the infant.[77-80]

In 2 multicenter cohort studies, van Veenendaal et al[81,82] used models of family integrated care (FICare) in the NICU. They assessed a care model with paternal mental health outcomes and a care model with stress in mothers of preterm infants. In the studies, families were placed in single-family rooms, which allowed for couplet care rather than the standard open-bay units in a traditional NICU setting. Mental health outcomes of mothers and fathers were assessed in this setting, with both reporting a significant reduction in stress scores at discharge from the NICU compared to parents in open-bay units getting standard neonatal care. On assessments of mother-newborn separation, they found that mothers were more present and participated more in neonatal care when they were provided with single-family rooms. Fathers reported similar experiences in participation of care.

Waiting for diagnostic testing results and anticipating the prognosis of the care recipient can be stressful for caregivers. In a multicenter study of parents of neonates with seizures, respondents suggested that medical professionals communicate effectively with parents, validate their experiences, and provide support and resources in a family-centered care approach. A partnership between parents and medical professionals could be very beneficial to all those involved.[83]

Parents of infants experiencing severe perinatal asphyxia are especially vulnerable to severe psychological trauma from the physical and psychological separation during therapeutic hypothermia (TH). Parents reported that the NICU staff played the most significant role in whether they were able to interact with and parent their babies during care activities such as diapering, temperature checks, and bathing.[84] Craig et al[85] conducted semistructured interviews of 15 families who reported their experiences as traumatic, filled with descriptive images of intensive life-saving medical procedures, pain, shivering from TH, and loss of opportunities to feed, hold, and bond with their infants.

TRAUMA-INFORMED CARE

Sanders and Hall[86] detailed a plan for ways that clinical and nonclinical staff in the NICU can support parents and prevent further traumatization after the birth event. By implementing the Substance Abuse and Mental Health Services Administration (SAMHSA)'s principles for trauma-informed care with applications derived from the Interdisciplinary Recommendations for Psychosocial Support of NICU Parents[87] and Trauma-Informed Care in the NICU,[88] parents are provided with empathy, support, and bonding opportunities with their infant. The types of strategies in the plan include reuniting the family as soon as possible after the birth or traumatic event, allotting privacy in single-family rooms; medical professionals providing clear, concise language that is free of medical jargon and using empathetic tones; allowing parents access to medical records; allowing the parents' presence during rounds; offering peer-to-peer support; nurses taking the role of mentor and letting the parents participate in care activities; parents being supported and encouraged in their role; and making sure that all families feel welcomed and are treated equally with culturally effective care.[86] Implementing trauma-informed care principles in the healthcare setting will enable caregivers to receive the support and understanding needed to prevent PTSD, depression, and anxiety.

HIE CAREGIVERS

Caregivers of those with HIE are under immense stress and pressure when caring for the patient and while fulfilling other aspects of day-to-day life. The intense nature of the caregiver's role lends itself to extreme stress and conflict. As role engulfment ensues, the caretaker can experience mental illness, physical illness, sleep deprivation, and fatigue from the impact of stress and care burden as they strive to meet the demands of caring for individuals with HIE. Implementing trauma-informed care principles detailed in the previous section will help ensure that the best care can be afforded to the patient. When the caregiver's health is affected, the care recipient often does not receive care reflective of the best outcomes possible.

In the TREND Community Voice Report (CVR)[89] on HIE, the artificial intelligence (AI) analytics engine, Krystie$_{TM}$, analyzed real-life conversations on social media to understand concerns in the HIE community. Using quantitative analysis with natural language processing (NLP), the themes important to caregivers were extracted from conversation data to better understand topics and areas of interest for further research. Given the limitation of the Sarnat Score Scale[19] in offering only 3 classifications on how a neonate presents at birth, a better understanding of the complexities of diagnosis and prognosis as the child develops remains an unmet need that the TREND community is exploring in the HIE community.[89]

A survey conducted on participants in the HIE community identified key themes relevant to communication and parental involvement during their stay in the NICU. Themes were identified as setting for communication, content/clarity of language, immediate and longitudinal support, clinician time and scheduling, valuing the parent role, and physical presence and touch.[90] In a call for trauma-informed care for caregivers of patients with HIE, 2 articles point to the need to implement this approach for parents to provide physical and emotional safety during their journey with medical professionals and staff in the clinical setting. In alignment with the themes detailed above, there was a need for clinicians to use clear, empathetic language that was free of medical jargon. Parents are vulnerable to being retraumatized with abrupt, uncaring, and harsh language about their infant. They need to feel that they can trust and collaborate with the medical staff so that they feel empowered. Face-to-face communication is essential because it provides them with a sense of caring. Written documentation about HIE should be offered to them so they can read it later at a time when they are ready to take in the information in a meaningful way. To build trust in the recipient's physicians, parents requested to hear terms regarding prognosis and diagnosis directly, instead of finding out information later on their own (ie, via the internet).[4,90]

CARE TRANSITIONS

One unmet need of the HIE community is providing support for parents as they transition home after the post-event/acute-care period (B. Pilon, personal oral communication, April 13, 2022). This stage can be filled with joy at going home, yet intense fear in realizing that they no longer have full support from hospital staff. In addition, navigating specialist appointments, therapies, other health services, early intervention requests, financial and insurance applications, job responsibilities, daycare for special needs infants, and care of siblings; finding peer-to-peer support; and facing other challenges are all-consuming changes in their lives of the caregivers.

Few studies have pursued this unmet need in rare and chronic disease communities. Mitchell et al[91] interviewed caregivers and patients and identified 3 outcomes they thought would make a difference in transitions of care: that medical professionals would take an interest and care about their needs, the healthcare system would be held accountable, and they would feel prepared to implement care plans at home. Transition services they felt would make a difference were medical providers using empathetic, caring language; the ability of medical staff and social workers to anticipate what the patient would need for self-care at home; engaging in collaborative discharge planning; providing credible information; and no gaps in care services after they are discharged and return home. In an effort to bridge the gap between hospital to home care, Project ACHIEVE[92] (Achieving Patient-Centered Care and Optimized Health In Care Transitions by Evaluating the Value of Evidence) was advanced to understand what outcomes and transitions were most important to caregivers and patients. This pilot will serve as the foundation for Project ACHIEVE's national survey to enroll more than 10,000 caregivers, patients, and medical providers.[91]

CONCLUSION

The intense nature of the caregiver's role leads to extreme stress and conflict for parents and guardians in the HIE community. The caregivers often experience trauma very early during the birth/event, and support systems are critical to caregiver and patient outcomes. Health-related and overall QoL are significantly lower for HIE caregivers than for parents of healthy children. As role engulfment ensues, the caretaker can experience mental illness, physical illness, sleep deprivation, and fatigue from the impact of stressors and care burden as they strive to meet the demands of caring for individuals with HIE. Fulfilling their other responsibilities and interpersonal relationships can be highly challenging for the caregiver.

Recurring themes identified in several studies of rare and chronic disease caregivers were the need for supportive care in the form of a family-centered approach and trauma-informed care to educate medical professionals on the nuances of and difficulties that caregivers face while caring for patients of HIE. Caregivers have consistently called for empathetic and caring tones from the medical providers as well as face-to-face conversations and access to credible information on their child's condition. The need to "always be the expert" is draining for caregivers; they need to be able to rely on physicians to keep up to date on the latest treatments. There is also a need to put behavioral therapies and strategies in place for the care recipient to help ease strains on the caregiver. Once burden is ameliorated for the caregiver, patient outcomes improve.

Transition of care from the NICU/PICU to home is difficult for parents. Caregivers want to be supported by being offered peer-to-peer support, respite care, information on HIE, coordination of care, and assistance finding other services related to navigating insurance companies and finances. By gleaning insights into the needs of caregivers, mental health professionals will be able to develop and implement strategies to best support them along their journey.

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