Prader-Willi Syndrome

Community Voice Report

VOLUME 2, ISSUE 1 - JUNE 2023

Justice Faith, PWS Community Ambassador

DISEASE CATEGORY

NEUROLOGICAL

ENDOCRINE

TREND Community™

Turning Anecdotes Into Evidence™

Actionable Community Insights

The Role of Evidence in Progress

The pace of progress is always accelerating. Innovations in technology, combined with regulatory incentives, are helping biotechs and pharmaceutical companies bring therapeutics and medical devices to patients faster than ever.

Unfortunately, most innovations are limited to finding treatments for diseases that are already well understood—that is, innovation in the rare disease space is lagging. In fact, 95% of the 10,000+ rare diseases have no approved treatments.

True understanding of rare diseases is the bottleneck. That's why the data and insights we capture from real patient voices are paramount to innovation. Our work unveils greater insights into disease presentation, symptoms, comorbidities, patient burden, and larger patterns. Ultimately, it is this holistic understanding that accelerates the development and approval of new therapeutics for which our communities are desperately waiting.

TREND's Real-World Impact

From Community Voice Reports to peer-reviewed journals, the insights we glean from community conversations are translating to real-world impact. Visit our website to view posters, reports, abstracts, and other publications that we've co-created with our community partners.

"The Community Voice Report helped us evolve from a Facebook group to a respected organization that is making a real difference in the HIE community."

—Betsy Pilon,

Executive Director, HOPE for HIE

How It Works

Trusted, Invite-Only Partnerships

We establish trusted, long-term partnerships with invite-only online communities that are formed organically by people affected by rare, chronic, and emerging diseases.

Proprietary Analytics

We harness machine learning and natural language processing techniques using Krystie™, our proprietary analytics engine that captures the perspectives and experiences of people within these trusted communities.

Evidence Acceleration

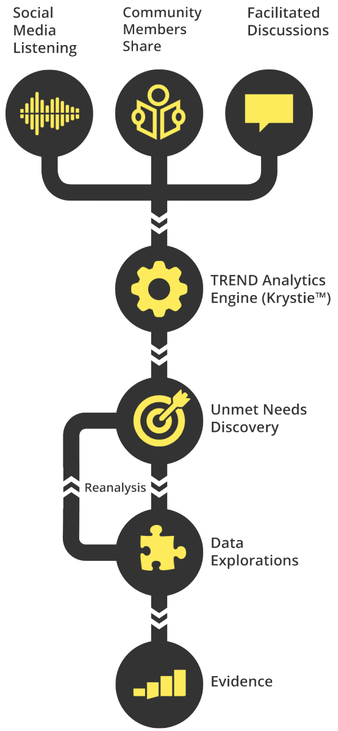
We discover insights on disease impacts and unmet needs. Our Community Voice Report and other real-world evidence can be leveraged for many different audiences and objectives.

Sponsors Use TREND Data To:

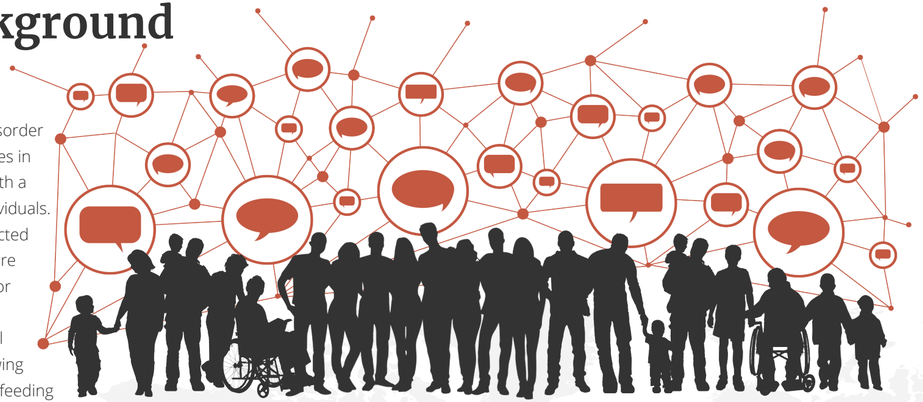
- Capture insights earlier and faster
- Understand the patient/caregiver journey
- Launch relevant awareness campaigns
- Identify community leaders and influencers
- Discover underrecognized disease impacts
- Include the patient voice at all stages

Communities Use TREND Data To:

- Enable shared decision-making
- Strengthen advocacy efforts
- Inform FDA & other regulatory agencies
- Build communities' unique vocabulary
- Discover underrecognized disease impacts
- Ensure biotech and pharma hear their voices



Analysis Background



Prader-Willi syndrome (PWS) is a life-threatening, neuroendocrine genetic disorder caused by the loss of expression of genes in paternal chromosome 15q11.2-q13,[1] with a prevalence of 1/10,000 to 1/30,000 individuals. Most cases are sporadic and not connected to family history. Recognized subtypes are deletion, maternal uniparental disomy, or imprinting defect.[2] PWS begins affecting individuals in utero, with decreased fetal movement and polyhydramnios.[3] Following birth, symptoms include hypotonia and feeding difficulties during infancy, developmental delays, endocrine abnormalities, short stature, high pain threshold, sleep disruptions, abnormal body composition, and—the hallmark symptom—hyperphagia.[4] In the absence of necessary interventions, morbid obesity and increased risk of mortality will result for the individual.[5] Now standard of care, human growth hormone (hGH) therapy was approved in 2000 for PWS to normalize height, improve body composition, and reduce developmental delays.[1]

Commonly reported behavioral symptoms are anxiety, compulsive behaviors, temper tantrums, aggression, and self-injury; these behaviors often arise in early childhood and persist throughout the lifespan.[6] The complications of PWS affect the personal safety, social interactions, and overall quality of life of the person with PWS, as well as the entire family.[5] However, with earlier diagnosis, intervention, and therapies—such as hGH—quality of life and various domains of functioning have improved greatly for those with PWS.

23,457
POSTS
SHARED

149,270
COMMENTS
ELICITED

MAR 2012 - APR 2023
DATE RANGE

By analyzing conversations on social media, we were able to glean insights into how the PWS community—including the person with PWS, their caregivers, and their families—is affected by this disorder and what their unmet needs and concerns are.

TREND analyzed 5 social media data sources for this report. All sources were private Facebook groups dedicated to PWS:

PWS Lovebugs | Birth to 2 years old

PWSA | USA Birth to 3 years old

PWSA | USA 3-5 years old

PWSA | USA 6-12 years old

PWSA | USA Parents of teens and older

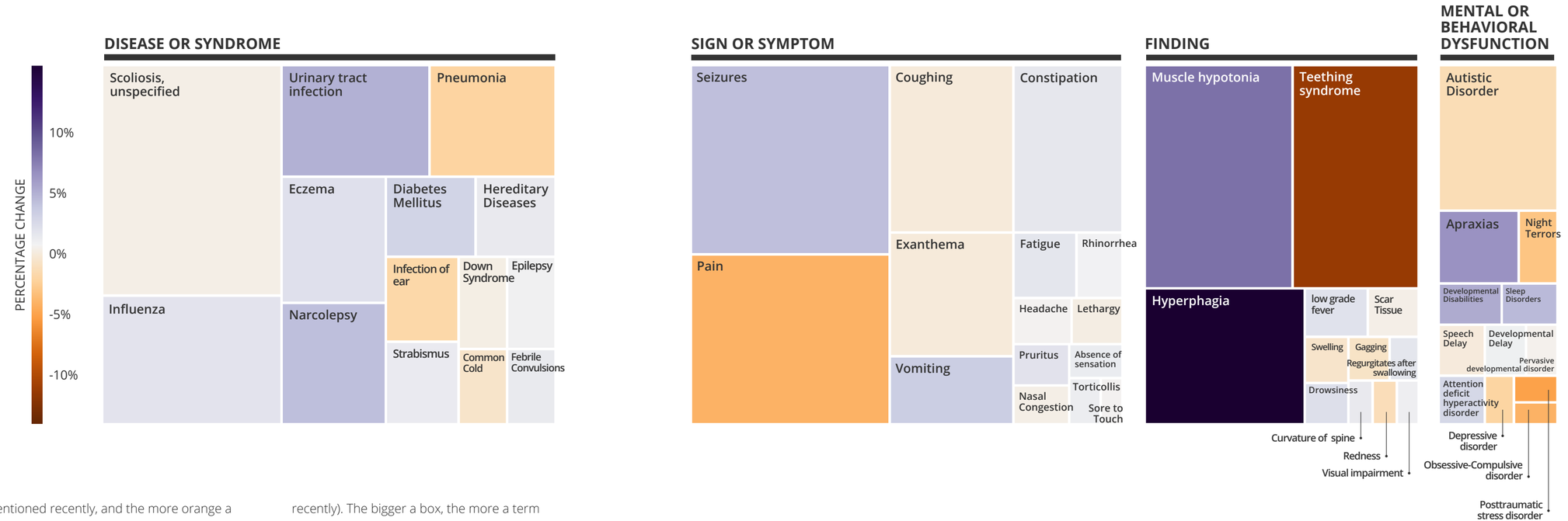
> ***Being a part of an online community makes being a rare parent not feel so lonely.***
>
> *— Community Member*

Trending Clinical Concepts

PWS is a complex disorder that affects many aspects of physical, cognitive, and behavioral development. The severity and manifestation of symptoms can vary greatly among individuals. To enhance our understanding of this disease, we analyze the most discussed terms and concepts from the social-media data sources and observe how they shift over time. Using this approach, we can pave the way for the development of more targeted and effective treatments.

Krystie uses the Unified Medical Language System (UMLS), a comprehensive knowledge resource for healthcare and biomedical researchers developed by the National Library of Medicine, to organize the symptoms and disease impacts discussed by the community into broad categories that encompass specific topics, specialties, or aspects of patient care called clinical domains.

The Tree map contains the most frequently mentioned clinical domains and their relative concepts, with Disease at 44.3%, Sign or Symptom at 28.1%, Finding at 18.9%, and Mental or Behavior Dysfunction at 8.7%. The map is colored by the percentage of mentions recently (2020-2023) vs historically (2012-2015). The more purple a concept, the more it was mentioned recently, and the more orange a concept, the more it was mentioned historically (e.g., 5% increase in Seizures mentions recently, 3% decrease in Pneumonia mentions recently). The bigger a box, the more a term was mentioned overall (e.g., Muscle hypotonia mentions were the highest in Findings).

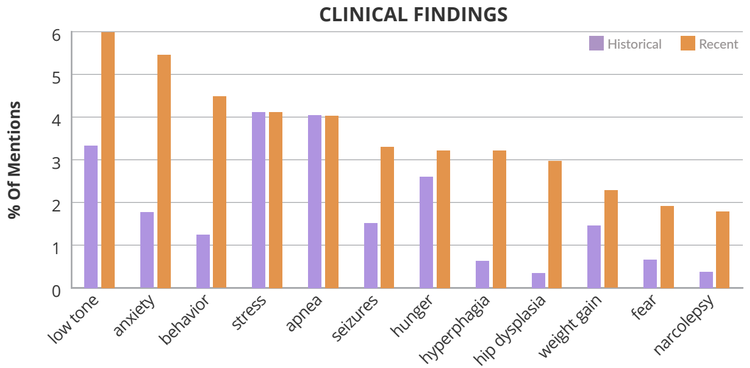


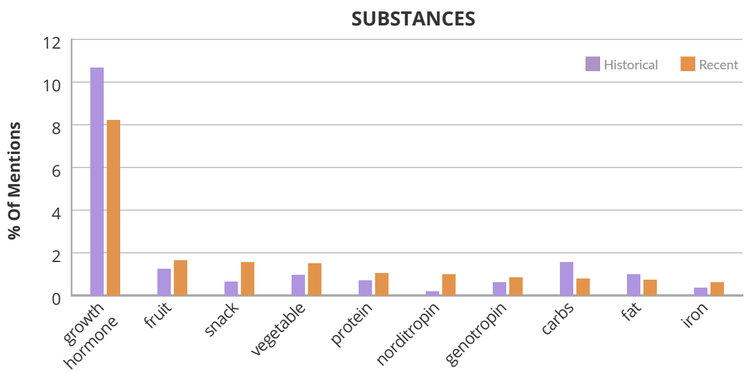
Top Clinical Findings and Substances

TREND's engine is trained to identify terms related to clinical language. Through this process, we can see the most frequently mentioned clinical concepts across clinical/medical domains. Two overarching clinical categories are presented here: Clinical Findings and Substances. "Clinical Finding" refers to any sign, symptom, or other phenomenon related a disease and its presentation. "Substances" refers to any medication, biomarker, food, or other physical matter that was mentioned.

The top figure to the right illustrates the most common clinical findings discussed historically (2012-2015) vs recently (2020-2023) across all domains.

The bottom figure to the right illustrates the most common substances discussed historically (2012-2015) vs recently (2020-2023).



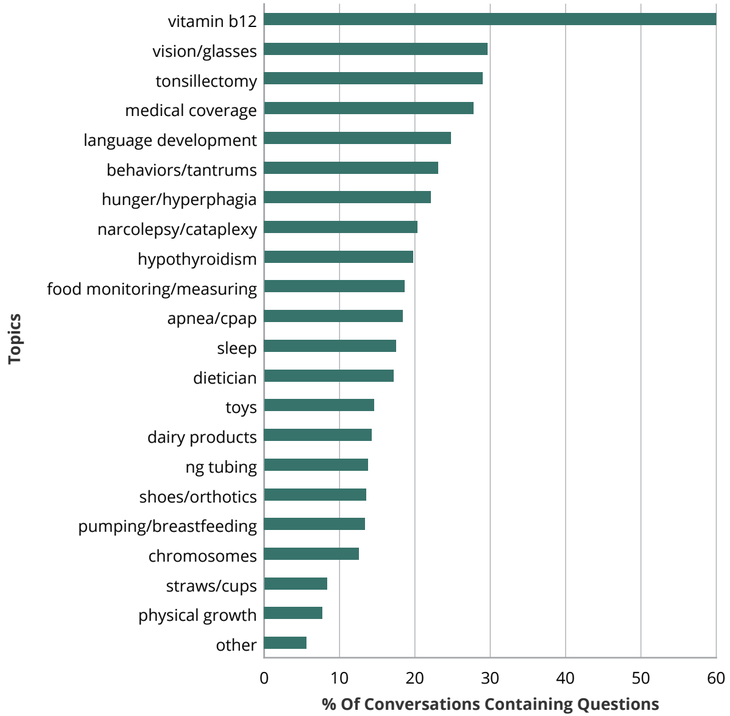


Frequently Asked Questions

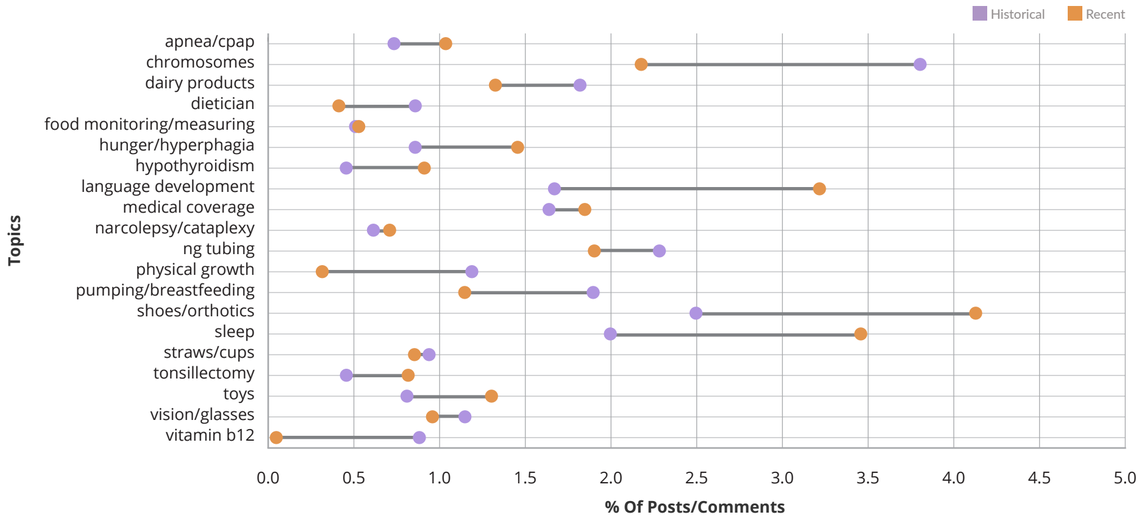
Community members often turn to their online support groups to find answers. Their questions can provide us with insights into the unmet needs of the community. We analyzed the most frequently discussed topics to determine what proportion of those conversations included questions.

This figure shows the highest-frequency topics (y-axis) and the percentage of conversations that included questions (x-axis). For example, 60% of all conversations about vitamin b12 involved a question.

It is notable that only 5.59% of all other topics discussed combined included questions. Therefore, this list gives us insight into possible gaps in resources and the community's need for education and support.



Shifts in Conversation Over Time



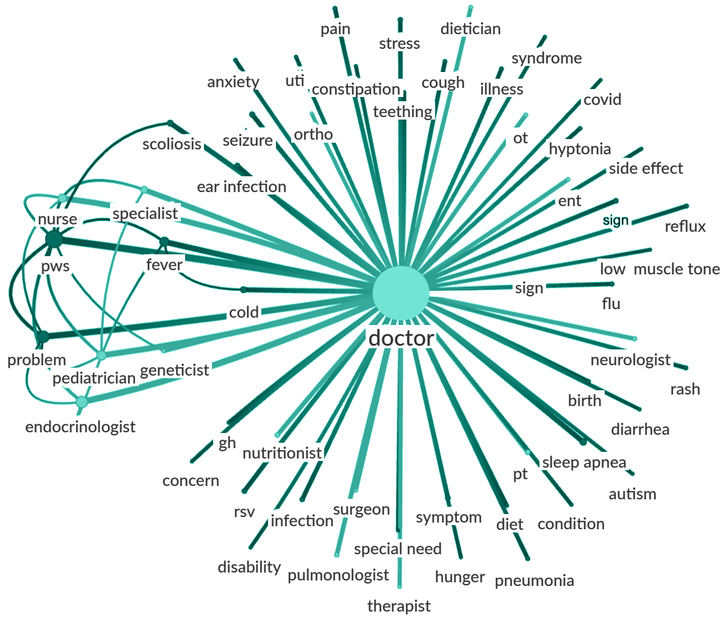
Medical advancements have the potential to profoundly impact and reshape the characteristics of diseases over time. By actively listening to the community, we can gain valuable insights into these shifts when they happen.

Krystie clusters language with similar meaning that appears together often. This process is called topic modeling. This figure shows the most frequent conversation topics and their shifts historically vs recently.

We see in the figure that the topics that have experienced the largest growth in conversations include *sleep, shoes/orthotics, language development,* and *hunger/hyperphagia*.

Network Analysis

This figure reflects the doctor network across PWS communities, providing a general indication of the clinical findings that might be most frequently discussed with medical professionals. In this network, we see reference to both acute (e.g., *fever, cold, rsv*) and chronic/ long-term (e.g., *low tone, special need, scoliosis*) findings. We are also able to see the most frequently mentioned medical professionals (e.g., *pediatrician, endocrinologist*).



Discovering Unmet Needs

Underrecognized Burdens

People living with PWS can experience significant disruptions in their daily routines, social relationships, and work/school. Because of the complexity of this syndrome, much is not known about the factors driving these issues. The community's conversations shed light on the wide-reaching effects of these and other issues.

Mental Health and Behavior

Although hyperphagia has been thought of as the hallmark feature of PWS, many families describe the behavioral and mental health aspects as being the most challenging in their and their loved one's daily lives. Obsessive-compulsive behaviors, anxiety, and tendency toward age-inappropriate reactions (e.g., temper tantrums) make it difficult for both the person with PWS and their caregiver(s) to navigate various activities and environments. These issues are not yet well understood or managed. A total of 10.9% of all conversations were related to mental health, with anxiety, stress, and fear being the top 3 mental health terms.

Sleep Disturbances

Even though clinicians and families are aware of the need for early nighttime sleep studies to address sleep apnea and hGH monitoring, few understand the need for continued monitoring and treatment of symptoms that may be related to those often seen in narcolepsy (e.g., falls, fatigue, lethargy). By actively listening to community needs on social media around falling and daytime sleepiness, TREND was able to bring the data to pharma to drive a clinical trial for pitolisant in PWS. Further awareness and diagnosis for clinicians regarding sleep issues in PWS are needed to address sleep concerns.

Appropriate Endpoints for Clinical Trials

Clinical trials that result in new therapeutics for PWS are greatly needed, but even those that have shown some degree of efficacy and safety have failed to receive FDA approval. In addition to accommodations for acknowledged limitations for PWS trials, such as small sample size (making it difficult to achieve sufficient statistical power), the community needs better instruments to adequately measure treatment effects and calls for the FDA to recognize such endpoints. Drugs such as DCCR (diazoxide choline) have been explored in clinical trials and shown effectiveness but will require regulatory flexibility to obtain approval.

> ***"We had all of the food locked up and he was rattling the cabinets and stealing food at school, screaming for food at home."***
>
> *— Community Member*

Appendix

Endnotes

1 Butler MG, Miller JL, Forster JL, et al. Prader-Willi syndrome - clinical genetics, diagnosis and treatment approaches: an update. *Curr Pediatr Rev.* 2019;15(4):207-244. doi:10.2174/1573396315666190716120925

2 Butler MG, Hartin SN, Hossain WA, et al. Molecular genetic classification in Prader-Willi syndrome: a multisite cohort study. *J Med Genet.* 2019;56(3):149-153. doi:10.1136/jmedgenet-2018-105301

3 Traisrisilp K, Sirikunalai P, Sirilert S, Chareonsirisuthigul T, Tongsong T. Cardiac rhabdomyoma as a possible new prenatal sonographic feature of Prader-Willi syndrome. *J Obstet Gynaecol Res.* 2022;48(1):239-243. doi:10.1111/jog.15073

4 Cassidy SB, Schwartz S, Miller JL, Driscoll DJ. Prader-Willi syndrome. *Genet Med.* 2012;14(1):10-26. doi:10.1038/gim.0b013e31822bead0

5 Shelkowitz E, Gantz MG, Ridenour TA, et al. Neuropsychiatric features of Prader-Willi syndrome. *Am J Med Genet A.* 2022;188(5):1457-1463. doi:10.1002/ajmg.a.62662

6 Schwartz L, Caixàs A, Dimitropoulos A, et al. Behavioral features in Prader-Willi syndrome (PWS): consensus paper from the International PWS Clinical Trial Consortium. *J Neurodev Disord.* 2021;13(1):25. doi:10.1186/s11689-021-09373-2

Acknowledgments

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About TREND Community

Founders & Values

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.

We Lead With Empathy
We lead and listen with empathy toward each other, our partners, and our communities.

We Amplify Voices
We believe that every voice has the power to make positive change.

We Are Transformational
We believe that our approach has the potential to change the lives of people living with rare, chronic, and emerging diseases and alter the course of disease management for the better.

Security

TREND secures all social data using state-of-the-art, private cloud servers. To protect community member privacy, conversation data from closed groups are anonymized, and the raw conversation data are never shared.

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).

Quotes

All quotes were provided by consenting community participants through online surveys, one-on-one interviews, or online focus groups. Names are not included to protect participants' privacy.

Data Ownership

Ownership of public posts or conversations from other social media platforms shared with TREND for analysis is subject to the social media platform's privacy policy, terms of service, and other applicable policies. TREND Community owns the results of our analysis and all other data and output we produce, including our Community Voice Reports.

License

TREND Community™
Turning Anecdotes Into Evidence™