

Appendix A: Search strings by database

PubMed:

("rare diseases"[MeSH Terms] OR "undiagnosed diseases"[MeSH Terms] OR "genetic diseases, inborn"[MeSH Terms] OR "genetic diseases, y linked"[MeSH Terms] OR "genetic diseases, x linked"[MeSH Terms] OR "chromosome aberrations"[MeSH Terms] OR "Congenital abnormalities"[MeSH Terms] OR "rare disease"[Text Word] OR "rare condition"[Text Word] OR "rare conditions"[Text Word] OR "undiagnosed disease"[Text Word] OR "genetic disease"[Text Word] OR "orphan disease"[Text Word] OR "rare diseases"[Text Word] OR "rare disorder"[Text Word] OR "rare disorders"[Text Word] OR "undiagnosed diseases"[Text Word] OR "genetic diseases"[Text Word] OR "orphan diseases"[Text Word] OR "genetic disorders"[Text Word] OR "genetic disorder"[Text Word] OR "rare cancer"[Text Word] OR "rare cancers"[Text Word] OR "rare tumors"[Text Word] OR "rare tumor"[Text Word] OR "congenital diseases"[Text Word] OR "congenital disease"[Text Word] OR "metabolic disease"[Text Word] OR "metabolic diseases"[Text Word] OR "inherited disorder"[Text Word] OR "inherited disorders"[Text Word] OR "rare health related events"[Text Word] OR "Congenital abnormalities"[Text Word] OR "congenital abnormality"[Text Word] OR "congenital defect"[Text Word] OR "congenital defects"[Text Word] OR "birth defects"[Text Word] OR "birth defect"[Text Word] OR "Rare Cardiac"[Text Word] OR "rare heart"[Text Word] OR "Rare Developmental"[Text Word] OR "Rare Genetic"[Text Word] OR "Rare Neurological"[Text Word] OR "rare brain"[Text Word] OR "Rare Hepatic"[Text Word] OR "rare liver"[Text Word] OR "Rare Respiratory"[Text Word] OR "rare lung"[Text Word] OR "Rare Urogenital"[Text Word] OR "rare Urologic"[Text Word] OR "Rare Skin"[Text Word] OR "Rare Renal"[Text Word] OR "rare kidney"[Text Word] OR "Rare Ophthalmic"[Text Word] OR "rare eye"[Text Word] OR "Rare Endocrine"[Text Word] OR "rare hormone"[Text Word] OR "Rare Hematological"[Text Word] OR "Rare Immunological"[Text Word] OR "rare immune"[Text Word] OR "rare blood"[Text Word] OR "Rare Bone"[Text Word] OR "Rare Neoplastic"[Text Word] OR "Rare Gynecological"[Text Word] OR "rare gynecologic"[Text Word] OR "Rare Obstetric"[Text Word] OR "Rare Gynecological"[Text Word] OR "Rare Allergic"[Text Word]) AND "english"[Language] AND ("social media"[MeSH Terms] OR "online social networking"[MeSH Terms] OR "internet based intervention"[MeSH Terms] OR "social media"[Text Word] OR "online support group"[Text Word] OR "online group"[Text Word] OR "online forum"[Text Word] OR "Facebook"[Text Word] OR "Youtube"[Text Word] OR "Instagram"[Text Word] OR "WeChat"[Text Word] OR "Tumblr"[Text Word] OR "TikTok"[Text Word] OR "Weibo"[Text Word] OR "google"[Text Word] OR "Reddit"[Text Word] OR "Twitter"[Text Word] OR "Pinterest"[Text Word] OR "MySpace"[Text Word] OR "Snapchat"[Text Word]) AND ("english"[Language] AND 2004/01/01:2021/12/31[Date - Publication]))

Web of Science:

TS= (((rare OR undiagnosed OR genetic OR orphan) NEAR/4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)) OR "rare disease" OR "undiagnosed disease" OR "genetic disease" OR "orphan disease" OR "rare diseases" OR "rare disorder" OR "rare disorders" OR "undiagnosed diseases" OR "genetic diseases" OR "orphan diseases" OR "genetic disorders" OR "genetic disorder" OR "rare cancer" OR "rare cancers" OR

"rare tumors" OR "rare tumor" OR "congenital diseases" OR "congenital disease" OR "metabolic disease" OR "metabolic diseases" OR "inherited disorder" OR "inherited disorders" OR "rare health related events" OR "congenital abnormalities" OR "congenital abnormality" OR "congenital defect" OR "congenital defects" OR "birth defects" OR "birth defect" OR "Rare Cardiac" OR "rare heart" OR "Rare Developmental" OR "Rare Sucking Swallowing" OR "Rare Inborn Errors Of Metabolism" OR "Rare Gastroenterological" OR "rare stomach" OR "Rare Genetic" OR "Rare Neurological" OR "rare brain" OR "Rare Abdominal Surgical" OR "Rare Hepatic" OR "rare liver" OR "Rare Respiratory" OR "rare lung" OR "Rare Urogenital" OR "rare Urologic" OR "Rare Surgical Thoracic" OR "Rare Skin" OR "Rare Renal" OR "rare kidney" OR "Rare Ophthalmic" OR "rare eye" OR "Rare Endocrine" OR "rare hormone" OR "Rare Hematological" OR "Rare Immunological" OR "rare immune" OR "Rare Systemic Rheumatological" OR "Rare Odontological" OR "rare tooth" OR "Rare Circulatory System" OR "rare blood" OR "Rare Bone" OR "Rare Otorhinolaryngological" OR "Rare Infertility" OR "Rare Neoplastic" OR "Rare Gynecological" OR "rare gynecologic" OR "Rare Obstetric" OR "Rare Gynecological" OR "Rare Surgical Maxillo-facial" OR "Rare Allergic" OR "Rare Teratologic" OR "Rare Transplant-Related") AND (TS=("social media" OR "online support group" OR "online group" OR "online forum" OR "facebook" OR "youtube" OR "instagram" OR "wechat" OR "tumblr" OR "tiktok" OR "weibo" OR "google+" OR "reddit" OR "twitter" OR "pinterest" OR "myspace" OR "google buzz" OR "snapchat"))

EMBASE:

('rare disease'/exp OR 'undiagnosed disease'/exp OR 'genetic disorder'/exp OR 'genetic and familial disorders'/exp OR 'congenital disorder'/exp OR (((rare OR undiagnosed OR genetic OR orphan) NEAR/4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)):ti,ab,kw) OR 'rare disease':ti,ab,kw OR 'undiagnosed disease':ti,ab,kw OR 'genetic disease':ti,ab,kw OR 'orphan disease':ti,ab,kw OR 'rare diseases':ti,ab,kw OR 'rare disorder':ti,ab,kw OR 'rare disorders':ti,ab,kw OR 'undiagnosed diseases':ti,ab,kw OR 'genetic diseases':ti,ab,kw OR 'orphan diseases':ti,ab,kw OR 'genetic disorders':ti,ab,kw OR 'genetic disorder':ti,ab,kw OR 'rare cancer':ti,ab,kw OR 'rare cancers':ti,ab,kw OR 'rare tumor':ti,ab,kw OR 'rare tumors':ti,ab,kw OR 'congenital diseases':ti,ab,kw OR 'congenital disease':ti,ab,kw OR 'metabolic disease':ti,ab,kw OR 'metabolic diseases':ti,ab,kw OR 'inherited disorder':ti,ab,kw OR 'inherited disorders':ti,ab,kw OR 'rare health related events':ti,ab,kw OR 'congenital abnormalities':ti,ab,kw OR 'congenital abnormality':ti,ab,kw OR 'congenital defect':ti,ab,kw OR 'congenital defects':ti,ab,kw OR 'birth defects':ti,ab,kw OR 'birth defect':ti,ab,kw OR 'rare cardiac':ti,ab,kw OR 'rare heart':ti,ab,kw OR 'rare developmental':ti,ab,kw OR 'rare sucking swallowing':ti,ab,kw OR 'rare inborn errors of metabolism':ti,ab,kw OR 'rare gastroenterological':ti,ab,kw OR 'rare stomach':ti,ab,kw OR 'rare genetic':ti,ab,kw OR 'rare neurological':ti,ab,kw OR 'rare brain':ti,ab,kw OR 'rare abdominal surgical':ti,ab,kw OR 'rare hepatic':ti,ab,kw OR 'rare liver':ti,ab,kw OR 'rare respiratory':ti,ab,kw OR 'rare lung':ti,ab,kw OR 'rare urogenital':ti,ab,kw OR 'rare urologic':ti,ab,kw OR 'rare surgical thoracic':ti,ab,kw OR 'rare skin':ti,ab,kw OR 'rare renal':ti,ab,kw OR 'rare kidney':ti,ab,kw OR 'rare ophthalmic':ti,ab,kw OR 'rare eye':ti,ab,kw OR 'rare endocrine':ti,ab,kw OR 'rare hormone':ti,ab,kw OR 'rare hematological':ti,ab,kw OR 'rare immunological':ti,ab,kw OR 'rare immune':ti,ab,kw OR 'rare systemic rheumatological':ti,ab,kw OR 'rare odontological':ti,ab,kw OR 'rare tooth':ti,ab,kw OR 'rare circulatory system':ti,ab,kw OR 'rare blood':ti,ab,kw OR 'rare bone':ti,ab,kw OR 'rare

otorhinolaryngological':ti,ab,kw OR 'rare infertility':ti,ab,kw OR 'rare neoplastic':ti,ab,kw OR 'rare gynecologic':ti,ab,kw OR 'rare obstetric':ti,ab,kw OR 'rare gynecological':ti,ab,kw OR 'rare surgical maxillo-facial':ti,ab,kw OR 'rare allergic':ti,ab,kw OR 'rare teratologic':ti,ab,kw OR 'rare transplant-related':ti,ab,kw) AND ('social media'/exp OR 'social media' OR 'online social network'/exp OR 'web-based intervention'/exp OR 'social media':ti,ab,kw OR 'online support group':ti,ab,kw OR 'online group':ti,ab,kw OR 'online forum':ti,ab,kw OR 'facebook':ti,ab,kw OR 'youtube':ti,ab,kw OR 'instagram':ti,ab,kw OR 'wechat':ti,ab,kw OR 'tumblr':ti,ab,kw OR 'tiktok':ti,ab,kw OR 'weibo':ti,ab,kw OR 'google+':ti,ab,kw OR 'reddit':ti,ab,kw OR 'twitter':ti,ab,kw OR 'pinterest':ti,ab,kw OR 'myspace':ti,ab,kw OR 'google buzz':ti,ab,kw OR 'snapchat':ti,ab,kw)

CINAHL (via Ebsco):

(MH "Rare Diseases") OR (MH "Undiagnosed Diseases") OR

(MH "Hereditary Diseases+") OR (MH "Genetic Diseases, X Linked+") OR (MH "Chromosome Aberrations+") OR (MH "Congenital, Hereditary, and Neonatal Diseases and Abnormalities+") OR TI (((rare OR undiagnosed OR genetic OR orphan) N4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)) OR "rare disease" OR "undiagnosed disease" OR "genetic disease" OR "orphan disease" OR "rare diseases" OR "rare disorder" OR "rare disorders" OR "undiagnosed diseases" OR "genetic diseases" OR "orphan diseases" OR "genetic disorders" OR "genetic disorder" OR "rare cancer" OR "rare cancers" OR "rare tumors" OR "rare tumor" OR "congenital diseases" OR "congenital disease" OR "metabolic disease" OR "metabolic diseases" OR "inherited disorder" OR "inherited disorders" OR "rare health related events" OR "congenital abnormalities" OR "congenital abnormality" OR "congenital defect" OR "congenital defects" OR "birth defects" OR "birth defect" OR "Rare Cardiac" OR "rare heart" OR "Rare Developmental" OR "Rare Sucking Swallowing" OR "Rare Inborn Errors Of Metabolism" OR "Rare Gastroenterological" OR "rare stomach" OR "Rare Genetic" OR "Rare Neurological" OR "rare brain" OR "Rare Abdominal Surgical" OR "Rare Hepatic" OR "rare liver" OR "Rare Respiratory" OR "rare lung" OR "Rare Urogenital" OR "rare Urologic" OR "Rare Surgical Thoracic" OR "Rare Skin" OR "Rare Renal" OR "rare kidney" OR "Rare Ophthalmic" OR "rare eye" OR "Rare Endocrine" OR "rare hormone" OR "Rare Hematological" OR "Rare Immunological" OR "rare immune" OR "Rare Systemic Rheumatological" OR "Rare Odontological" OR "rare tooth" OR "Rare Circulatory System" OR "rare blood" OR "Rare Bone" OR "Rare Otorhinolaryngological" OR "Rare Infertility" OR "Rare Neoplastic" OR "Rare Gynecological" OR "rare gynecologic" OR "Rare Obstetric" OR "Rare Gynecological" OR "Rare Surgical Maxillo-facial" OR "Rare Allergic" OR "Rare Teratologic" OR "Rare Transplant-Related") OR AB (((rare OR undiagnosed OR genetic OR orphan) N4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)) OR "rare disease" OR "undiagnosed disease" OR "genetic disease" OR "orphan disease" OR "rare diseases" OR "rare disorder" OR "rare disorders" OR "undiagnosed diseases" OR "genetic diseases" OR "orphan diseases" OR "genetic disorders" OR "genetic disorder" OR "rare cancer" OR "rare cancers" OR "rare tumors" OR "rare tumor" OR "congenital diseases" OR "congenital disease" OR "metabolic disease" OR "metabolic diseases" OR "inherited disorder" OR "inherited disorders" OR "rare health related events" OR "congenital abnormalities" OR "congenital abnormality" OR "congenital defect" OR "congenital defects" OR "birth defects" OR "birth

defect" OR "Rare Cardiac" OR "rare heart" OR "Rare Developmental" OR "Rare Sucking Swallowing" OR "Rare Inborn Errors Of Metabolism" OR "Rare Gastroenterological" OR "rare stomach" OR "Rare Genetic" OR "Rare Neurological" OR "rare brain" OR "Rare Abdominal Surgical" OR "Rare Hepatic" OR "rare liver" OR "Rare Respiratory" OR "rare lung" OR "Rare Urogenital" OR "rare Urologic" OR "Rare Surgical Thoracic" OR "Rare Skin" OR "Rare Renal" OR "rare kidney" OR "Rare Ophthalmic" OR "rare eye" OR "Rare Endocrine" OR "rare hormone" OR "Rare Hematological" OR "Rare Immunological" OR "rare immune" OR "Rare Systemic Rheumatological" OR "Rare Odontological" OR "rare tooth" OR "Rare Circulatory System" OR "rare blood" OR "Rare Bone" OR "Rare Otorhinolaryngological" OR "Rare Infertility" OR "Rare Neoplastic" OR "Rare Gynecological" OR "rare gynecologic" OR "Rare Obstetric" OR "Rare Gynecological" OR "Rare Surgical Maxillo-facial" OR "Rare Allergic" OR "Rare Teratologic" OR "Rare Transplant-Related") AND (MH "Social Media+") OR (MH "Online Social Networking") OR

(MH "Internet-Based Intervention") OR TI ("social media" OR "online support group" OR "online group" OR "online forum" OR "Facebook" OR "Youtube" OR "Instagram" OR "WeChat" OR "Tumblr" OR "TikTok" OR "Weibo" OR "Google+" OR "Reddit" OR "Twitter" OR "Pinterest" OR "MySpace" OR "Google Buzz" OR "Snapchat") OR AB ("social media" OR "online support group" OR "online group" OR "online forum" OR "Facebook" OR "Youtube" OR "Instagram" OR "WeChat" OR "Tumblr" OR "TikTok" OR "Weibo" OR "Google+" OR "Reddit" OR "Twitter" OR "Pinterest" OR "MySpace" OR "Google Buzz" OR "Snapchat")

PsycINFO (via ProQuest):

(MESH("rare diseases") OR MESH("undiagnosed diseases") OR MESH("genetic diseases, inborn") OR MESH("genetic diseases, Y-linked") OR MESH("genetic diseases, X-linked") OR MESH("chromosome aberrations") OR MESH("Congenital abnormalities") OR MAINSUBJECT.EXACT.EXPLODE("Genetic Disorders") OR MAINSUBJECT.EXACT.EXPLODE("Congenital Disorders") OR ((rare OR undiagnosed OR genetic OR orphan) N4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)) OR "rare disease" OR "undiagnosed disease" OR "genetic disease" OR "orphan disease" OR "rare diseases" OR "rare disorder" OR "rare disorders" OR "undiagnosed diseases" OR "genetic diseases" OR "orphan diseases" OR "genetic disorders" OR "genetic disorder" OR "rare cancer" OR "rare cancers" OR "rare tumors" OR "rare tumor" OR "congenital diseases" OR "congenital disease" OR "metabolic disease" OR "metabolic diseases" OR "inherited disorder" OR "inherited disorders" OR "rare health related events" OR "congenital abnormalities" OR "congenital abnormality" OR "congenital defect" OR "congenital defects" OR "birth defects" OR "birth defect" OR "Rare Cardiac" OR "rare heart" OR "Rare Developmental" OR "Rare Sucking Swallowing" OR "Rare Inborn Errors Of Metabolism" OR "Rare Gastroenterological" OR "rare stomach" OR "Rare Genetic" OR "Rare Neurological" OR "rare brain" OR "Rare Abdominal Surgical" OR "Rare Hepatic" OR "rare liver" OR "Rare Respiratory" OR "rare lung" OR "Rare Urogenital" OR "rare Urologic" OR "Rare Surgical Thoracic" OR "Rare Skin" OR "Rare Renal" OR "rare kidney" OR "Rare Ophthalmic" OR "rare eye" OR "Rare Endocrine" OR "rare hormone" OR "Rare Hematological" OR "Rare Immunological" OR "rare immune" OR "Rare Systemic Rheumatological" OR "Rare Odontological" OR "rare tooth" OR "Rare Circulatory System" OR "rare blood" OR "Rare

Bone" OR "Rare Otorhinolaryngological" OR "Rare Infertility" OR "Rare Neoplastic" OR "Rare Gynecological" OR "rare gynecologic" OR "Rare Obstetric" OR "Rare Gynecological" OR "Rare Surgical Maxillo-facial" OR "Rare Allergic" OR "Rare Teratologic" OR "Rare Transplant-Related") AND (MESH("social media") OR MESH("online social networking") OR MESH("internet based intervention") OR MAINSUBJECT.EXACT.EXPLODE("Social Media") OR MAINSUBJECT.EXACT.EXPLODE("Online Social Networks") OR MAINSUBJECT.EXACT.EXPLODE("Digital Interventions") OR "social media" OR "online support group" OR "online group" OR "online forum" OR "Facebook" OR "Youtube" OR "Instagram" OR "WeChat" OR "Tumblr" OR "TikTok" OR "Weibo" OR "Google+" OR "Reddit" OR "Twitter" OR "Pinterest" OR "MySpace" OR "Google Buzz" OR "Snapchat")

Communications & Mass Media Complete (via Ebsco):

(DE "GENETIC disorders" OR ((rare OR undiagnosed OR genetic OR orphan) N4 (disease OR diseases OR disorder OR disorders OR cancer OR cancers OR tumors OR tumor)) OR "rare disease" OR "undiagnosed disease" OR "genetic disease" OR "orphan disease" OR "rare diseases" OR "rare disorder" OR "rare disorders" OR "undiagnosed diseases" OR "genetic diseases" OR "orphan diseases" OR "genetic disorders" OR "genetic disorder" OR "rare cancer" OR "rare cancers" OR "rare tumors" OR "rare tumor" OR "congenital diseases" OR "congenital disease" OR "metabolic disease" OR "metabolic diseases" OR "inherited disorder" OR "inherited disorders" OR "rare health related events" OR "congenital abnormalities" OR "congenital abnormality" OR "congenital defect" OR "congenital defects" OR "birth defects" OR "birth defect" OR "Rare Cardiac" OR "rare heart" OR "Rare Developmental" OR "Rare Sucking Swallowing" OR "Rare Inborn Errors Of Metabolism" OR "Rare Gastroenterological" OR "rare stomach" OR "Rare Genetic" OR "Rare Neurological" OR "rare brain" OR "Rare Abdominal Surgical" OR "Rare Hepatic" OR "rare liver" OR "Rare Respiratory" OR "rare lung" OR "Rare Urogenital" OR "rare Urologic" OR "Rare Surgical Thoracic" OR "Rare Skin" OR "Rare Renal" OR "rare kidney" OR "Rare Ophthalmic" OR "rare eye" OR "Rare Endocrine" OR "rare hormone" OR "Rare Hematological" OR "Rare Immunological" OR "rare immune" OR "Rare Systemic Rheumatological" OR "Rare Odontological" OR "rare tooth" OR "Rare Circulatory System" OR "rare blood" OR "Rare Bone" OR "Rare Otorhinolaryngological" OR "Rare Infertility" OR "Rare Neoplastic" OR "Rare Gynecological" OR "rare gynecologic" OR "Rare Obstetric" OR "Rare Gynecological" OR "Rare Surgical Maxillo-facial" OR "Rare Allergic" OR "Rare Teratologic" OR "Rare Transplant-Related") AND (DE "SOCIAL media" OR DE "BACKCHANNELS (Social media)" OR DE "BLOGS" OR DE "COMPUTER bulletin boards" OR DE "ONLINE chat" OR DE "ONLINE social networks" OR DE "PODCASTS" OR DE "SOCIAL bookmarks" OR DE "WIKIS" OR DE "ONLINE social networks" OR DE "SOCIAL cataloging" OR "social media" OR "online support group" OR "online group" OR "online forum" OR "Facebook" OR "Youtube" OR "Instagram" OR "WeChat" OR "Tumblr" OR "TikTok" OR "Weibo" OR "Google+" OR "Reddit" OR "Twitter" OR "Pinterest" OR "MySpace" OR "Google Buzz" OR "Snapchat")

Appendix B: Codebook**Study Goal:**

Code	Definition	Example
Development of research methods	Study attempts to develop or refine research methods. This can include feasibility studies in using social media to recruit patients, comparisons between social media methods and traditional methods, and explorations of new ways to use social media for rare disease research.	“The aim of our study was to test whether a Web-based direct recruitment approach (patient-centric, PC) using social marketing strategies provides a viable option to the CoE recruitment method.” ¹
Evaluation of how social media is used	Study attempts to understand how social media is used within a rare disease community. This can include explorations of content within online support groups or Twitter hashtags or evaluations the quality or quantity of information available on social media.	“Our aim in this study was to conduct a descriptive and quantitative analysis of the use of a social media community for Hirschsprung’s Disease (HD).” ²
Evaluation of patient health status or outcomes	Study examines specific physical indicators, symptoms, or outcomes and is medically or clinically oriented.	“Patients with cleidocranial dysplasia (CCD) can have a congenital partial or total absence of the clavicle. The aim of this study was to evaluate the functional shoulder score in these patients.” ³
Evaluation of psychosocial needs of patient or caregivers	Study focuses on the mental or social health or needs of the patient or caregiver. This can include an exploration of barriers to care or attitudes around treatments.	“We surveyed parents of children with T13-18 who belong to support groups to describe their experiences and perspectives.” ⁴
Other	Does not fit into above codes.	

Disease(s) Studied:

Code	Definition	Example
Mixed rare and non-rare diseases	Sample contains both rare and non-rare diseases.	ALS, MS
Unspecified “rare diseases”	Sample is defined only as “rare disease” or “rare diseases.”	Rare diseases
Single rare disease	Sample is only one rare disease.	Cystic fibrosis
Subset of rare diseases	Sample is a subset of rare diseases.	Addison's Disease, Cushing's syndrome
Undiagnosed	Sample is undiagnosed disease.	Undiagnosed

Study Type:

Code	Definition	Example
Observational	Cohort study or case report that does not involve an intervention	“We analyzed the treatment information entered by patient members about the two drugs of

		interest, amitriptyline and modafinil, across five condition-based communities.” ⁵
Experimental	Study that involves an intervention created by the researchers	“Upon informed consent, participants were placed on an e-mail list with other group members— all comprising fathers of children (birth to 17 years) with a brain tumor. The network comprised three months of access to a closed online forum that was developed and hosted by AboutKidsHealth, the patient education group at The Hospital for Sick Children in Toronto, Canada.” ⁶
Cross-sectional	Study data not analyzed for change over time.	“We analyzed the treatment information entered by patient members about the two drugs of interest, amitriptyline and modafinil, across five condition-based communities.” ⁵
Longitudinal	Study data collected at multiple time points to observe change over time	“At enrollment, patients completed baseline surveys and a series of patient-reported outcome measures evaluating constructs affected by the disease and its treatment... Patients completed the electronic health status every 3 months after enrollment.” ⁷
Other	Does not fit into above codes.	

Methodology:

<i>Code</i>	<i>Definition</i>	<i>Example</i>
Survey	Online or paper survey	“This was a cross-sectional study using G Suite Google Platform and a netnographic analysis of interactions among patients with GTD who were members of FBGTD and were invited to participate in a survey from March 6 to October 5, 2017.” ⁸
Interview	In-person, phone, or video interview	“In each case, one or more caregivers (usually parents) were interviewed by a pediatric neurologist (KAM for 30 cases and GR for one). Each interview involved a thorough history surrounding seizure patterns and treatment responses, as well as a review of the pregnancy, delivery, developmental, general medical, and family histories.” ⁹

Content analysis	Content analysis of posts and/or comments on a social media site	“We analyzed all twitter posts (tweets) under the hashtag of #BPDCN during the study time period of May 22, 2016– March 1, 2017.” ¹⁰
Treatment study	Medically oriented clinical trial or natural history study	“After verbal consent, a study packet containing epidemiologic surveys [14,15], an Oragene DNA saliva kit (DNA Genotek Inc), study instructions, consent documents, health information release form, and prepaid return envelope were mailed to the participant’s home address.” ¹¹
Online intervention	Social media was created as an experimental, behavioral intervention	“Upon informed consent, participants were placed on an e-mail list with other group members— all comprising fathers of children (birth to 17 years) with a brain tumor. The network comprised three months of access to a closed online forum that was developed and hosted by AboutKidsHealth, the patient education group at The Hospital for Sick Children in Toronto, Canada.” ⁶
Other	Does not fit into above codes.	

Role of Social Media:

<i>Code</i>	<i>Definition</i>	<i>Example</i>
Primary data collection	The social media platform’s role is to collect data directly from social media users. Includes delivery of an online link from an outside platform into a social media group, site, or forum. Code will always be co-coded with “Recruitment.” because all identified studies that used social media for primary data collection also used social media to recruit participants. However, some studies used social media to recruit participants but did not use social media for data collection.	“Patients with NMOSD, who were members of a closed international Facebook Group, were recruited to complete an anonymous survey on REDCap. Participants were queried regarding demographic and NMOSD-related characteristics and PS history.” ¹²
Recruitment	Social media platform was used for recruitment for interview (in-person or phone), for paper-based based survey, for an online survey, or for clinical trial or other clinical study.	“Recruitment took place through the CTF website, NF-related Facebook groups, at the annual CTF Patient Forum, through NF clinics and the CTF volunteer network, and through word of mouth and social media.” ¹³

Secondary data analysis	The content of the social media platform was analyzed. Posts and/or comments in rare disease-specific groups, hashtags, sites, or forums were explored.	“This is a content analysis of three vascular diseases of differing degrees of rarity. Wall posts from Facebook patient support groups for May Thurner syndrome, thoracic outlet syndrome, and superior mesenteric artery syndrome were analyzed over a period of two years.” ¹⁴
Intervention delivery	Study involved an experimental intervention, including a clinical trial or the creation of online social media group or hashtag with the intention of studying rare disease patients.	“Interventional study for parents of adolescents with NF1 aged 13-18 years including 2 phases: (1) Creating Video Intervention/Prevention Assessment (VIA) visual narratives on smartphones about parenting a child with NF1; (2) Interacting on C@H, a secure, medically-moderated social media website, with phase 1 visual narratives and responses using video and text. C@H was evaluated qualitatively via semi-structured phone interviews at: enrollment (T0), after creating video narratives (T1), and after interacting with other parents on C@H (T2).” ¹⁵
Other	Does not fit into above codes.	

Justification for Social Media Sampling Frame:

<i>Code</i>	<i>Definition</i>	<i>Example</i>
Existing collaboration	Study authors worked with an existent rare disease organization or group.	“Recruitment was conducted via email and social media in partnership with epidermolysis bullosa patient advocacy organizations (Debra of America and EB Research Partnership) in the United States.” ¹⁶
Size/scope of users in community/platform	Study authors chose a social media platform due to its size, scope, or popularity.	“Facebook’s largest support group for caregivers of individuals with CS (629 members) was selected for study.” ¹⁷
Content or format of social media site is aligned with study goals	Study authors chose a social media platform because the format (videos, etc.) or type of data or information (e.g., group is unmoderated, information is public, participants are verified, etc.) were specific to study goals.	“This informal email correspondence was formalized into an email-based online support group hosted by a University of Chicago listserv in April 2010. Our research group invited all families in our Registry known to be affected by KATP-channel mutations. By design, all participants had an accurate, validated diagnosis of this unique form of diabetes. This enhances the

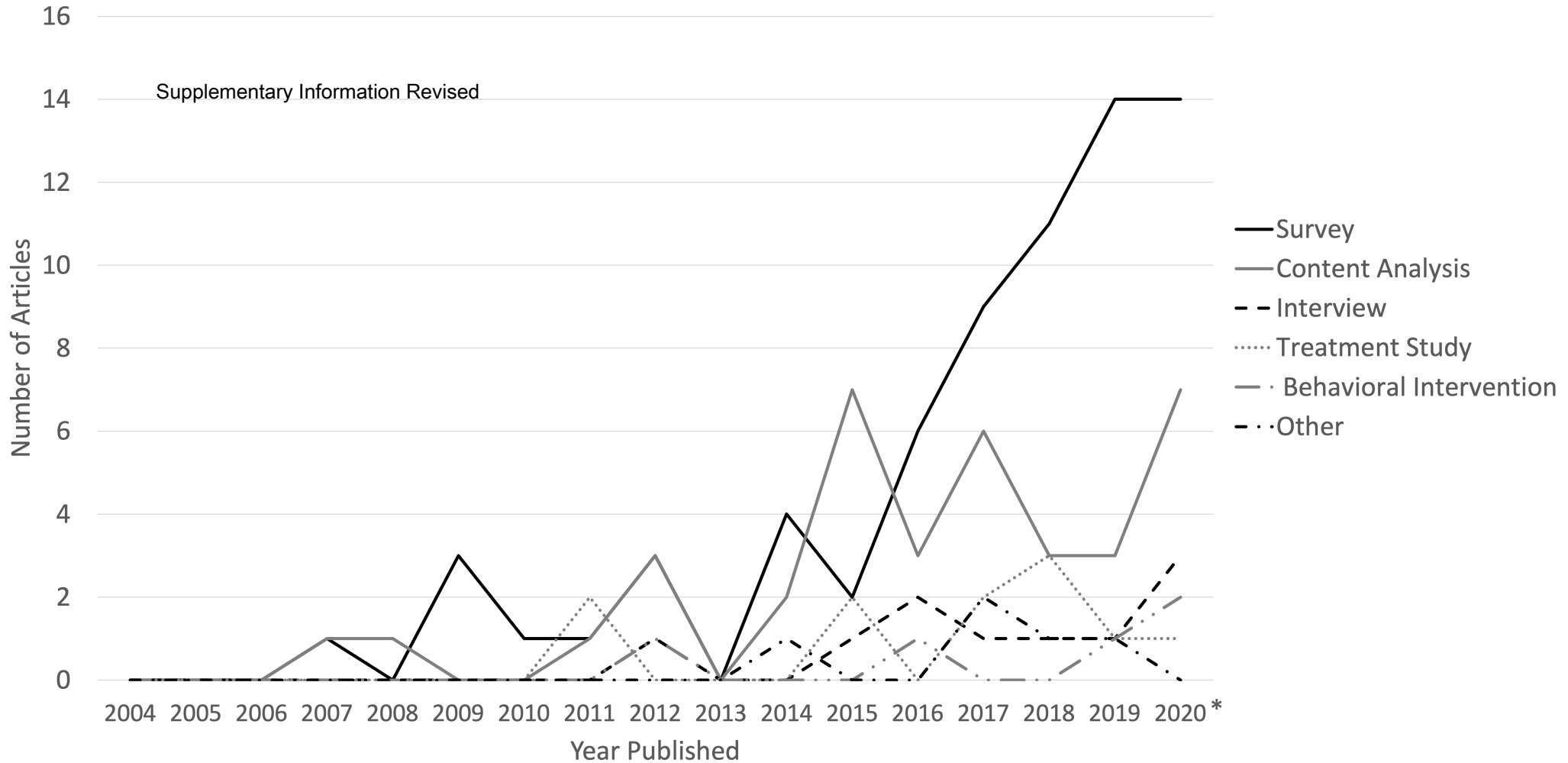
		internal validity and credibility of the study.” ¹⁸
Not reported/unclear	No clear justification for choice of social media platform	
Other	Does not fit into above codes.	

Reference List for Appendix B:

1. Krischer J, Cronholm PF, Burroughs C, et al. Experience With Direct-to-Patient Recruitment for Enrollment Into a Clinical Trial in a Rare Disease: A Web-Based Study. *J Med Internet Res.* 2017;19(2):e50. doi:10.2196/jmir.6798
2. Wittmeier K, Holland C, Hobbs-Murison K, et al. Analysis of a parent-initiated social media campaign for Hirschsprung’s disease. *J Med Internet Res.* 2014;16(12):e288. doi:10.2196/jmir.3200
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Figure S1: Study Method Frequency Over Time



* Includes only studies published between January 1st, 2020 and November 10th, 2020

Table S2: Diseases

Disease Name	Number of Articles (%)*
Cystic fibrosis	14 (11.3%)
Amyotrophic lateral sclerosis	7 (5.6%)
Blastic plasmacytoid dendritic cell neoplasm	4 (3.3%)
Huntington's disease	4 (3.3%)
Hirschsprung disease	3 (2.5%)
Myeloproliferative neoplasm	3 (2.5%)
Neurofibromatosis type 1	3 (2.5%)
Sickle cell disease	3 (2.5%)
Adult bladder exstrophy	2 (1.7%)
Anorectal malformation	2 (1.7%)
Autoimmune hepatitis	2 (1.7%)
Craniofacial microsomia	2 (1.7%)
Dermatofibrosarcoma protuberans	2 (1.7%)
Ehlers-Danlos syndrome	2 (1.7%)
Epithelioid hemangioendothelioma	2 (1.7%)
Esophageal Atresia	2 (1.7%)
Ewing's sarcoma	2 (1.7%)
Fontan-associated protein-losing enteropathy	2 (1.7%)
Hereditary hemorrhagic telangiectasia	2 (1.7%)
Idiopathic subglottic stenosis	2 (1.7%)
Microtia	2 (1.7%)
Osteosarcoma	2 (1.7%)
Plastic bronchitis	2 (1.7%)
Spontaneous coronary artery dissection	2 (1.7%)
Tracheoesophageal fistula	2 (1.7%)
Trisomy 13	2 (1.7%)
Trisomy 18	2 (1.7%)
16p11.2 deletion syndrome	1 (0.8%)
22q11 deletion syndrome	1 (0.8%)
6q11-q15 deletion	1 (0.8%)
Achalasia	1 (0.8%)
Addison's disease	1 (0.8%)
Aggressive angiomyxoma	1 (0.8%)
Albinism	1 (0.8%)
Anderson-Fabry disease	1 (0.8%)
Angiosarcoma	1 (0.8%)
Arthrogryposis multiplex congenita	1 (0.8%)
CHARGE syndrome	1 (0.8%)
Childhood brain tumor	1 (0.8%)
Cholesteatoma	1 (0.8%)
Chondrosarcoma	1 (0.8%)
Cleidocranial dysplasia	1 (0.8%)
Congenital diaphragmatic hernia	1 (0.8%)

Congenital disorders of glycosylation (LeQCDG)	1 (0.8%)
Congenital heart disease	1 (0.8%)
Costello syndrome	1 (0.8%)
Craniosynostosis	1 (0.8%)
Cushing's syndrome	1 (0.8%)
Desmoid fibromatosis	1 (0.8%)
Dravet syndrome	1 (0.8%)
Emanuel syndrome	1 (0.8%)
Epidermolysis bullosa	1 (0.8%)
Epispadias	1 (0.8%)
Epithelioid sarcoma	1 (0.8%)
Fragile X syndrome	1 (0.8%)
Gaucher disease	1 (0.8%)
Gestational trophoblastic disease	1 (0.8%)
Giant axonal neuropathy	1 (0.8%)
Goldenhar syndrome	1 (0.8%)
Granulomatosis with polyangiitis	1 (0.8%)
Hemophilia	1 (0.8%)
Hereditary ovarian cancer	1 (0.8%)
Hypospadias	1 (0.8%)
KAT6A syndrome	1 (0.8%)
KATP channel-related monogenic neonatal diabetes	1 (0.8%)
Koolen-de Vries syndrome	1 (0.8%)
Leiomyosarcoma	1 (0.8%)
Lesch-Nyhan disease	1 (0.8%)
Liposarcoma	1 (0.8%)
Lynch Syndrome	1 (0.8%)
Madducci syndrome	1 (0.8%)
Marfan syndrome	1 (0.8%)
May Thurner syndrome	1 (0.8%)
Mayer–Rokitansky–Küster–Hauser syndrome	1 (0.8%)
Mucopolysaccharidosis type 1	1 (0.8%)
Multiple endocrine neoplasia type 1	1 (0.8%)
Multiple hereditary exostoses	1 (0.8%)
Multiple myeloma	1 (0.8%)
Neuroendocrine carcinoma of the cervix	1 (0.8%)
Neurofibromatosis type 2	1 (0.8%)
Neuromyelitis optica spectrum disorder	1 (0.8%)
NGLT1 deficiency	1 (0.8%)
Ollier disease	1 (0.8%)
Persistent hyperplastic primary vitreous	1 (0.8%)
Pompe disease	1 (0.8%)
Pontine cap dysplasia	1 (0.8%)
Prader-Willi syndrome	1 (0.8%)

Pulmonary fibrosis	1 (0.8%)
Rare kidney disease	1 (0.8%)
Retinitis pigmentosa	1 (0.8%)
Sagittal Craniosynostosis	1 (0.8%)
Sanfilippo syndrome	1 (0.8%)
Schwannomatosis	1 (0.8%)
Spinal muscular atrophy	1 (0.8%)
Superior mesenteric artery syndrome	1 (0.8%)
Systemic lupus erythematosus	1 (0.8%)
Tenosynovial giant cell tumors	1 (0.8%)
Transverse myelitis	1 (0.8%)
Turner syndrome	1 (0.8%)
Xeroderma pigmentosum	1 (0.8%)

*Some articles reported on more than one disease, so percentages sum to >100.

Table S3: Disease Categories

Disease Category	Number of Articles (%)*
Congenital and Genetic Diseases	71 (59.2%)
Digestive Diseases	38 (31.2%)
Nervous System Diseases	28 (23.3%)
Lung Diseases	23 (19.2%)
Male Reproductive Diseases	19 (15.8%)
Rare Cancers	18 (15.0%)
Musculoskeletal Diseases	17 (14.1%)
Blood Diseases	14 (11.6%)
Eye Diseases	14 (11.6%)
Kidney and Urinary Diseases	14 (11.6%)
Skin Diseases	12 (10.0%)
Chromosome Disorders	8 (6.7%)
Endocrine Diseases	8 (6.7%)
Heart Diseases	7 (5.8%)
Ear, Nose, and Throat Diseases	6 (5.0%)
Mouth Diseases	6 (5.0%)
Female Reproductive Diseases	5 (4.2%)
Metabolic Disorders	5 (4.2%)
Autoimmune / Autoinflammatory diseases	3 (2.5%)
Connective Tissue Diseases	3 (2.5%)
Immune System Diseases	2 (1.7%)
Hereditary Cancer Syndromes	1 (0.8%)
Undiagnosed	1 (0.8%)
"Rare diseases" unspecified	5 (4.2%)

*Many articles reported on more than one disease category, so percentages sum to >100.

Table S4: Countries of Participants

Country	Number of Papers (%)
United States	36 (30.0%)
United Kingdom	20 (16.7%)
Canada	18 (15.0%)
Australia	16 (13.3%)
New Zealand	9 (7.5%)
Germany	6 (5.0%)
Spain	6 (5.0%)
Italy	5 (4.2%)
Finland	4 (3.3%)
Netherlands	4 (3.3%)
Norway	4 (3.3%)
Croatia	3 (2.5%)
France	3 (2.5%)
India	3 (2.5%)
China	2 (1.7%)
Japan	2 (1.7%)
South Africa	2 (1.7%)
Switzerland	2 (1.7%)
Algeria	1 (0.8%)
Belgium	1 (0.8%)
Brazil	1 (0.8%)
Chile	1 (0.8%)
Columbia	1 (0.8%)
Denmark	1 (0.8%)
District of Columbia	1 (0.8%)
Ireland	1 (0.8%)
Israel	1 (0.8%)
Lithuania	1 (0.8%)
Nigeria	1 (0.8%)
Peru	1 (0.8%)
Philippines	1 (0.8%)
Puerto Rico	1 (0.8%)
Sweden	1 (0.8%)
The UAE	1 (0.8%)
Tunisia	1 (0.8%)
Turkey	1 (0.8%)
Venezuela	1 (0.8%)
Zimbabwe	1 (0.8%)