

THE LANCET

Digital Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Miao BY, Sushil M, Xu A, et al. Characterisation of digital therapeutic clinical trials: a systematic review with natural language processing. *Lancet Digit Health* 2024; **6**: e222–29.

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Supplementary figures

Table S1. Number of search results returned from ClinicalTrials.gov for each DTx-associated term.

Search term	Number of studies
"digital therapeutic"	76
"digital therapy"	33
"digital therapies"	33
"mobile health"	1598
"smartphone"	3219
"smart phone"	3219
"digital intervention"	156
"mobile platform"	53
"mobile app"	1834
"mobile device"	462
"study app"	48
"digital treatment"	27
"android"	401
" app."	1265
" app,"	766
"digital tablet"	21
" ios"	340
"iphone"	219
"smart watch"	83
"smartwatch"	140
"virtual reality"	1747
"video game"	598
"digital health"	388
"mobile video"	12
"digital platform"	120
"software intervention"	7
"software treatment"	8



Figure S1. Missing values in DTx clinical trials for each data field. Only data fields where at least 1 trial contains a missing value is shown. Black bars indicate missing data.

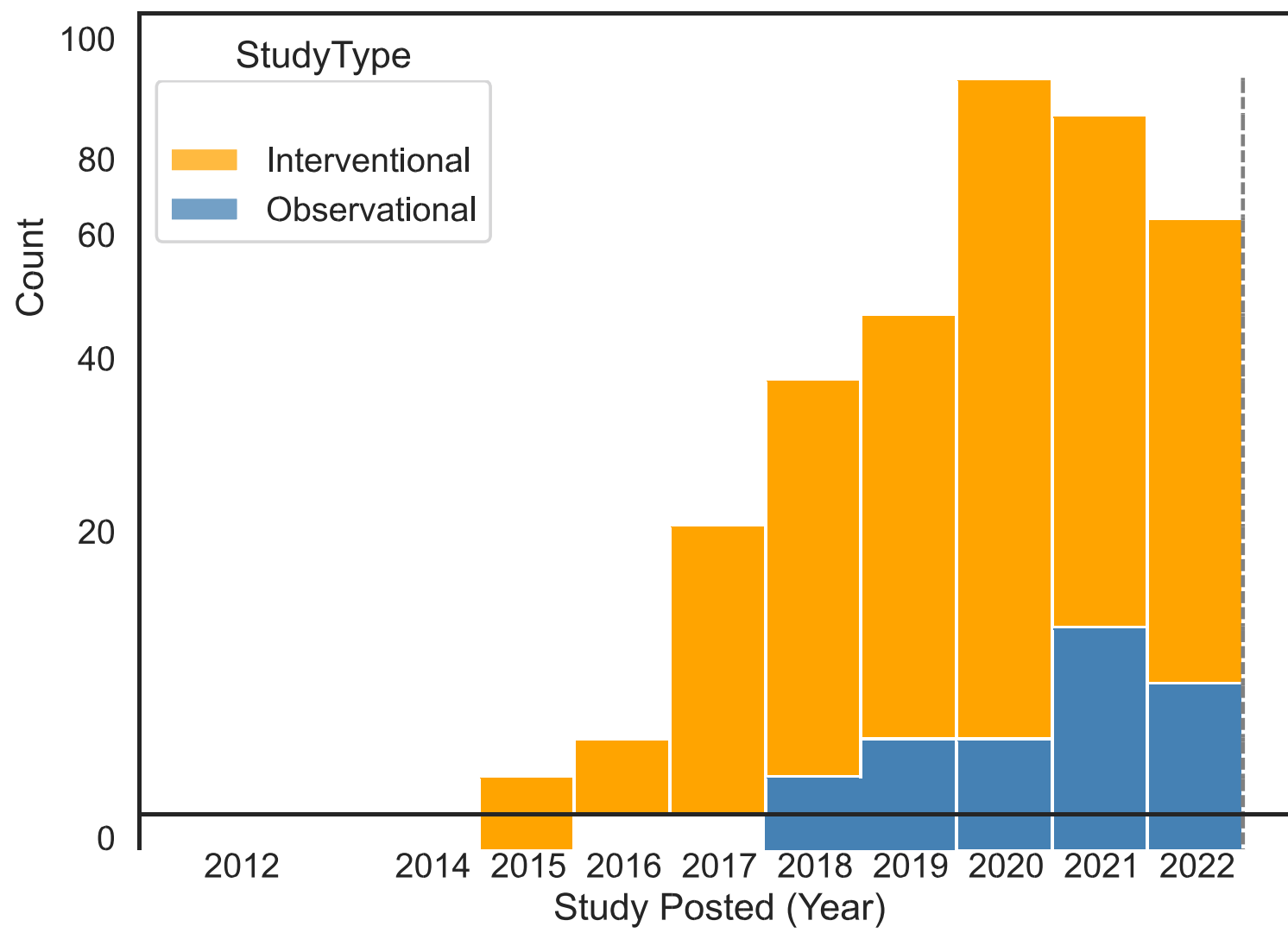


Figure S2. Distribution of study post dates for digital therapeutic clinical trials.

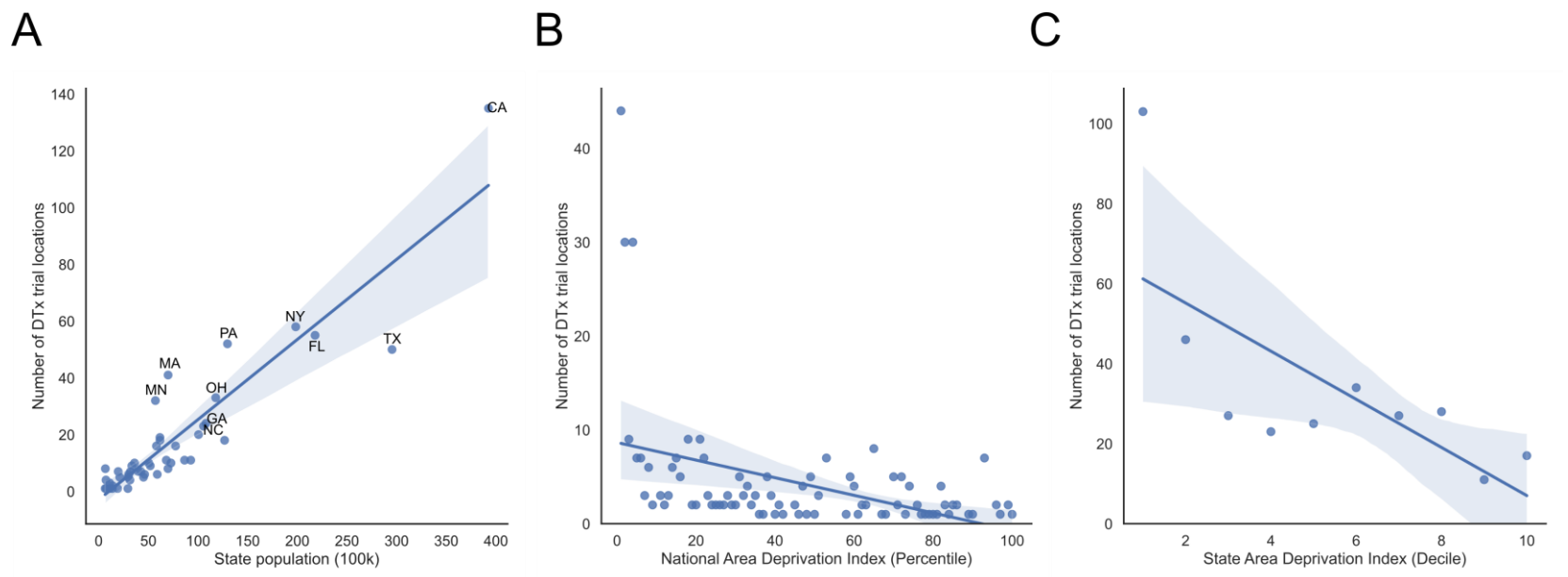


Figure S3: Correlation between number of DTx clinical trial locations and geographic characteristics. A) Correlation between number of DTx clinical trials and state population. The top 10 states with the highest number of DTx clinical trials are labeled. Within the top 5 states, we also looked at the relationship between number of DTx trial locations and area deprivation index (ADI) at the B) national level and C) state level. The national ADI is calculated relative to other zip codes in the United States, while the state ADI is relative to other zip codes in the state. Higher ADI scores at both the national and state level indicate greater socioeconomic disadvantage.

Table S2: Incorrect MeSH branches selected by SciSpacy EntityLinker.

Clinical Trial	Condition (ClinicalTrials.gov)	MeSH branch (SciSpacy EntityLinker)	Incorrect (“N”) or “Multiple” possible MeSH Branches
NCT03934658	['PostTraumatic Stress Disorder' 'Sleep Disorder' 'Stress Disorder' 'Sleep Initiation and Maintenance Disorders' 'Combat Disorders' 'Nightmares Associated With Chronic Post-Traumatic Stress Disorder' 'Nightmare' 'Nightmares, REM-Sleep Type']	Psychological Phenomena	N
NCT03828656	['PostTraumatic Stress Disorder' 'Sleep Disorder' 'Stress Disorder' 'Sleep Initiation and Maintenance Disorders' 'Combat Disorders' 'Nightmares Associated With Chronic Post-Traumatic Stress Disorder' 'Nightmare' 'Nightmares, REM-Sleep Type']	Psychological Phenomena	N
NCT03795987	['Stress Disorders, Post-Traumatic' 'Combat Disorders' 'Ptd' 'Nightmare' 'Nightmares, REM-Sleep Type' 'Nightmare Disorder With Associated Non-Sleep Disorder']	Psychological Phenomena	N
NCT04040387	['Stress Disorders, Post-Traumatic' 'Combat Disorders' 'Ptd' 'Nightmare' 'Nightmares, REM-Sleep Type' 'Nightmare Disorder With Associated Non-Sleep Disorder']	Psychological Phenomena	N
NCT04897074	['Attention Deficit Hyperactivity Disorder']	Psychological Phenomena	N
NCT04418076	['HIV/AIDS' 'Cocaine Use']	Organic Chemicals	N
NCT04846777	['Generalized Anxiety Disorder']	Investigative Techniques	N
NCT03748264	['Sleep Disordered Breathing']	Psychological Phenomena	N
NCT05077644	['Post-partum Depression']	Urogenital Diseases	N
NCT04364256	['Autologous Hematopoietic Stem Cell Transplant']	Biological Factors	N
NCT04684823	['Cystic Fibrosis' 'Adherence, Medication']	Digestive System Diseases	N
NCT03047720	['Nocturnal Enuresis']	Heterocyclic Compounds	N
NCT03649074	['Attention Deficit Hyperactivity Disorder']	Psychological Phenomena	N
NCT03678402	['High Risk for Falling']	Investigative Techniques	N
NCT04429009	['Thoracic Surgery' 'Respiratory Therapy']	Health Occupations	N
NCT05147987	['Insufficient Lactation']	Urogenital Diseases	N
NCT05454813	['System Validation']	Hemic and Immune Systems	N
NCT04584970	['Scoliosis Idiopathic' 'Pain, Postoperative']	Infections	N
NCT05150197	['Visual Field Defect, Peripheral']	Diagnosis	N
NCT04416555	['Postoperative Pain']	Therapeutics	N
NCT04268901	['Phlebotomy' 'Orthopedics' 'Radiology' 'Pain' 'Anxiety' 'Virtual Reality' 'Allergy' 'Gastroenterology']	Immune System Diseases	N
NCT04175444	['Visual Field Defect, Peripheral']	Diagnosis	N
NCT04025814	['Attention Deficit Hyperactivity Disorder']	Psychological Phenomena	N
NCT04857515	['Smoking Cessation' 'Smoking Behaviors' 'Smoking Reduction' 'Smoking, Cigarette' 'Smoking' 'Nicotine Dependence']	Behavior and Behavior Mechanisms	Multiple
NCT05365607	['Posttraumatic Stress Disorder' 'Cardiovascular Diseases' 'Autonomic Dysfunction' 'Vascular Stiffness' 'Nightmare' 'Endothelial Dysfunction']	Mental Disorders	Multiple
NCT03340311	['Gestational Diabetes Mellitus']	Urogenital Diseases	Multiple
NCT04808609	['Smoking Cessation' 'Smoking' 'Smoking Behaviors' 'Smoking Reduction' 'Smoking, Tobacco' 'Smoking, Cigarette' 'Hiv' 'HIV/AIDS']	Behavior and Behavior Mechanisms	Multiple
NCT04609514	['HIV/AIDS' 'Smoking Cessation' 'Tobacco Use Disorder']	Behavior and Behavior Mechanisms	Multiple
NCT04854798	['Covid19' 'Cytokine Storm' 'Inflammation']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04701489	['Covid19' 'Cytokine Storm' 'Inflammation']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04838925	['Chronic Pain' 'Opioid Use']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04217551	['Cardiac Arrest, Out-Of-Hospital' 'Hypothermia, Induced' 'Hypoxia-Ischemia, Brain']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04332718	['Stroke' 'Atrial Fibrillation']	Nervous System Diseases	Multiple
NCT03519451	['Depression' 'Tobacco Use Disorder' 'Current Every Day Smoker']	Behavior and Behavior Mechanisms	Multiple
NCT03475147	['Scotoma']	Nervous System Diseases	Multiple
NCT04465682	['Urine Detectable Acute and Chronic Diseases']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04297969	['Amblyopia Bilateral' 'Hyperopia of Both Eyes' 'Astigmatism Bilateral' 'Accommodation Disorder']	Nervous System Diseases	Multiple
NCT04607460	['Chronic Low-back Pain' 'Mastectomy' 'Lumpectomy' 'Migraine']	Nervous System Diseases	Multiple
NCT04659564	['Breast Cancer Related Lymphedema' 'Lymphedema of Upper Arm' 'Lymphedema' 'Quality of Life']	Hemic and Lymphatic Diseases	Multiple

NCT03506568	['Medication Adherence' 'Glaucoma']	Behavior and Behavior Mechanisms	Multiple
NCT04205370	['Sleep' 'Pregnancy Complications']	Psychological Phenomena	Multiple
NCT04721067	['Hiv' 'Insomnia']	Nervous System Diseases	Multiple
NCT05212129	['Functional Gastrointestinal Disorders' 'Hypermobile Ehlers-Danlos Syndrome' 'Postural Orthostatic Tachycardia Syndrome' 'Autonomic Nervous System Disease' 'Autonomic Nervous System Imbalance']	Nervous System Diseases	Multiple
NCT05099874	['Sickle Cell Disease' 'Attention Deficit' 'Cognitive Deficit in Attention']	Hemic and Lymphatic Diseases	Multiple
NCT05427734	['Suicide' 'Suicide, Attempted' 'Suicidal Ideation' 'Alcohol Use Disorder' 'Alcoholism' 'Alcohol Abuse' 'Screening and Brief Interventions']	Chemically-Induced Disorders	Multiple
NCT03905863	['Diabetic Foot Ulcer' 'Surgical Wound']	Cardiovascular Diseases	Multiple
NCT05378399	['HIV Infections' 'Substance Use' 'Adherence, Medication' 'Adherence, Treatment']	Behavior and Behavior Mechanisms	Multiple
NCT05130112	['Small Airway Disorders' 'COPD']	Pathological Conditions, Signs and Symptoms	Multiple
NCT04169282	['Tracheobronchomalacia']	Musculoskeletal Diseases	Multiple
NCT05473702	['Heart Disease Chronic' 'Pulmonary Disease, Chronic Obstructive' 'Blood Pressure' 'Heart Rhythm Disorder']	Respiratory Tract Diseases	Multiple
NCT05212363	['Compression; Vein' 'Compression; Artery' 'Sedentary Behavior' 'DVT of Legs']	Behavior and Behavior Mechanisms	Multiple

Table S3: Studies with conditions not mapped to MeSH headings by SciSpacy EntityLinker.

Clinical Trial	Study Official Title	Condition
NCT04887922	The Effect of Preoperative and Postoperative Incentive Spirometry in Patients Undergoing Major Abdominal Surgery	Abdominal Surgery
NCT04910139	A User Study of the Soniflow System for Nasal Congestion Relief	Nasal Congestion
NCT02091882	OSMITTER 316-13-206A Substudy: A Substudy to Measure the Accuracy of Ingestible Event Marker (IEM) Detection by the Medical Information Device #1 (MIND1) System and Determine the Latency Period	Device Latency
NCT05052281	Promoting Healthy Brain Development Via Prenatal Stress Reduction: An Innovative Precision Medicine Approach	Prenatal Stress
NCT05099614	Naloxone Administration Via Auto -injection in Healthy Volunteers	Overdose Antidote
NCT05199844	Accuracy of Apple Watch to Measure Cardiovascular Indices in Patients With Cardiac Diseases: Observational Study	Apple Watch

Table S4: Keyword components comprising each inclusion criteria topic.

Topic name	MeSH Category	Proportion	Components
Clinical factors	Pathological Conditions, Signs and Symptoms	21/38 (55.3%)	pain, months, sleep, scale, 10
	Nervous System Diseases	31/66 (47.0%)	pain, score, month, months, insomnia treatment, medication, score, stable, month
	Mental Disorders	11/24 (45.8%)	
	Nutritional and Metabolic Diseases	15/38 (39.5%)	smbg, participants, months, prior, therapy
	Cardiovascular Diseases	8/24 (33.3%)	score, states, resident, vasc, patients treatment, 20th, percentile, systemic, having
	Neoplasms	5/17 (29.4%)	
Informed consent	Behavior and Behavior Mechanisms	9/32 (28.1%)	pain, usa, average, baseline, reported
	Nutritional and Metabolic Diseases	24/38 (63.2%)	consent, informed, willing, provide, hipaa consent, informed, provide, willing, required
	Behavior and Behavior Mechanisms	18/32 (56.2%)	
	Neoplasms	9/17 (52.9%)	consent, informed, written, provide, willing
	Nervous System Diseases	32/66 (48.5%)	consent, informed, provide, willing, able
	Pathological Conditions, Signs and Symptoms	16/38 (42.1%)	consent, informed, provide, willing, signed
Age (>18)	Mental Disorders	9/24 (37.5%)	consent, informed, provide, willing, able
	Cardiovascular Diseases	6/24 (25.0%)	informed, consent, ascertained, able, valid
	Behavior and Behavior Mechanisms	23/32 (71.9%)	18, years, age, old, ages
	Nutritional and Metabolic Diseases	25/38 (65.8%)	years, age, 18, old, male
	Pathological Conditions, Signs and Symptoms	25/38 (65.8%)	18, years, age, aged, old
	Cardiovascular Diseases	14/24 (58.3%)	18, years, age, older, male
	Nervous System Diseases	38/66 (57.6%)	years, age, 18, old, aged
Smartphone access	Mental Disorders	13/24 (54.2%)	years, 18, age, 22, older
	Neoplasms	6/17 (35.3%)	years, 18, age, old, mole
	Nutritional and Metabolic Diseases	18/38 (47.4%)	smartphone, device, mobile, phone, compatible
	Neoplasms	8/17 (47.1%)	smartphone, access, recorded, audio, mobile
	Behavior and Behavior Mechanisms	12/32 (37.5%)	smartphone, android, access, iphone, ios smartphone, iphone, game, android, controller
	Mental Disorders	7/24 (29.2%)	
	Cardiovascular Diseases	6/24 (25.0%)	smartphone, plan, data, wi, fi
English fluency	Nervous System Diseases	11/66 (16.7%)	smartphone, access, device, holds, license comfortable, complete, zoom, conferencing, web
	Pathological Conditions, Signs and Symptoms	2/38 (5.3%)	
	Behavior and Behavior Mechanisms	11/32 (34.4%)	english, fluency, read, speaking, literacy
	Nutritional and Metabolic Diseases	12/38 (31.6%)	english, read, speaking, speak, write
	Neoplasms	5/17 (29.4%)	english, read, speak, speaking, write english, speaking, read, understand, spanish
	Pathological Conditions, Signs and Symptoms	10/38 (26.3%)	
	Cardiovascular Diseases	6/24 (25.0%)	english, speaking, read, write, speak
English fluency	Mental Disorders	6/24 (25.0%)	english, speaking, proficient, read, language
	Nervous System Diseases	15/66 (22.7%)	english, speaking, read, spanish, speak

Table S5: Keyword components comprising each exclusion criteria topic.

Topic name	MeSH Category	Proportion	Components
Medical history	Mental Disorders	23/24 (95.8%)	disorder, suicidal, use, current, months
	Pathological Conditions, Signs and Symptoms	33/38 (86.8%)	disorder, history, severe, current, use
	Cardiovascular Diseases	20/24 (83.3%)	heart, weeks, patients, cardiac, disorder
	Nervous System Diseases	55/66 (83.3%)	disorder, history, severe, disease, months
	Nutritional and Metabolic Diseases	31/38 (81.6%)	insulin, disease, disorder, months, investigator
	Behavior and Behavior Mechanisms	26/32 (81.2%)	disorder, current, smoking, suicidal, treatment
	Neoplasms	13/17 (76.5%)	disorder, history, care, therapy, psychiatric
Pregnancy	Nutritional and Metabolic Diseases	21/38 (55.3%)	pregnant, pregnancy, women, female, feeding
	Pathological Conditions, Signs and Symptoms	12/38 (31.6%)	pregnant, pregnancy, teeth, women, face
	Behavior and Behavior Mechanisms	9/32 (28.1%)	pregnant, planning, face, pregnancy, comfortable
	Nervous System Diseases	18/66 (27.3%)	pregnant, pregnancy, women, breastfeeding, potential
	Neoplasms	4/17 (23.5%)	pregnant, adults, populations, vulnerable, prisoners
	Mental Disorders	5/24 (20.8%)	pregnant, pregnancy, teenagers, cycles, menstrual
	Cardiovascular Diseases	3/24 (12.5%)	postpartum, wfbmc, center, location, birth
Allergies or other skin conditions	Neoplasms	5/17 (29.4%)	cancer, documented, skin, patients, hematologic
	Nutritional and Metabolic Diseases	11/38 (28.9%)	skin, cell, allergy, basal, neoplasms
	Pathological Conditions, Signs and Symptoms	7/38 (18.4%)	skin, cancer, carcinoma, sores, hardware
	Behavior and Behavior Mechanisms	4/32 (12.5%)	skin, fragile, dermatologic, intact, oozing
	Cardiovascular Diseases	3/24 (12.5%)	wound, patches, surface, adhesive, skin
	Mental Disorders	2/24 (8.3%)	cancers, skin, cvd, preexisting, angiomas
	Nervous System Diseases	5/66 (7.6%)	allergic, skin, known, tapes, reaction
Cardiovascular metrics	Cardiovascular Diseases	8/24 (33.3%)	mmhg, diastolic, cm, baseline, dl
	Nutritional and Metabolic Diseases	9/38 (23.7%)	mmhg, pressure, 60, ml, min
	Pathological Conditions, Signs and Symptoms	4/38 (10.5%)	inches, 79, clots, obesity, circumference
	Nervous System Diseases	5/66 (7.6%)	mmhg, 60, diastolic, 30, cm
	Neoplasms	1/17 (5.9%)	mass, 35, bmi, index, body
	Mental Disorders	1/24 (4.2%)	tsh, thyroid, pcp, mu, values
Ability to provide informed consent	Neoplasms	5/17 (29.4%)	consent, informed, sign, willing, inability
	Cardiovascular Diseases	3/24 (12.5%)	consent, provide, informed, inability, unwilling
	Nervous System Diseases	8/66 (12.1%)	consent, informed, provide, written, unable
	Nutritional and Metabolic Diseases	4/38 (10.5%)	consent, informed, inability, provide, unwillingness
	Pathological Conditions, Signs and Symptoms	3/38 (7.9%)	consent, informed, provide, inability, unable
	Behavior and Behavior Mechanisms	2/32 (6.2%)	informed, consent, inability, provide, unwillingness
	Mental Disorders	1/24 (4.2%)	consent, informed, adults, unable, written

Table S6: Incorrect values from manual assessment of topic modeling in a subset of 200 inclusion eligibility criteria.

NCTid	Inclusion Criteria (Preprocessed)	BERTopic cluster	Expected cluster
NCT03142932	agree anticipate living baltimore 2 months	Clinical factors	Other
NCT04380415	u.s. resident	Clinical factors	Other
NCT03214224	1	Clinical factors	NA
NCT03418129	served military branches army navy marines air force coast guard october 2001.	Clinical factors	Other
NCT03335800	current resident united states time eligibility screening defined self reported state residence 50 states united states district columbia.	Clinical factors	Other
NCT04524598	residing usa duration 5 week	Clinical factors	Other
NCT04268914	4. children normal range development recruited study. assessed report parents. rationale excluding patients developmental delay cognitive impairments children react stressors surgery differently children developmental delay. unclear children use preparation programs interventions included likely responses baseline outcome measures differ children normal developmental parameters.	Clinical factors	Ability to provide informed consent
NCT04253691	unable complete forms implement treatment cognitive impairment mmse<26	Clinical factors	Ability to provide informed consent
NCT04607460	able speak understand english 6 access computer tablet home email address.	Ability to provide informed consent	English fluency
NCT03335800	valid phone number associated iphone ascertained self report.	Ability to provide informed consent	Smartphone access
NCT03338036	holds valid driver s license	Smartphone access	Other

Table S7: Incorrect values from manual assessment of topic modeling in a subset of 200 exclusion eligibility criteria.

NCTid	Inclusion Criteria (Preprocessed)	BERTopic cluster	Expected cluster
NCT05263037	members household	Medical history	Other
NCT04394754	incarceration	Medical history	Other
NCT03528174	hematocrit 36 men 32 women.	Pregnancy	Cardiovascular metrics
NCT04479735	refuses lidocaine 2.5 prilocaine 2.5 cream use excluded study.	Medical history	Ability to provide informed consent
NCT05293275	injury eyes face neck impedes comfortable use virtual reality	Medical history	Medical history
NCT04797611	agree use approved contraception method entirety trial	Medical history	Ability to provide informed consent
NCT05263037	injury eyes face neck prevents comfortable use vr.	Pregnancy	Ability to provide informed consent
NCT04906603	loss consciousness greater 30 minutes	Cardiovascular metrics	Medical history
NCT04230486	volunteers unable complete tasks understand instructions	Medical history	Ability to provide informed consent
NCT05112432	legal commitment treatment medical guardianship provision guardianship order court order allow guardian consent research	Medical history	Ability to provide informed consent
NCT03315286	employee direct relative employee investigational site sponsor	Medical history	Ability to provide informed consent
NCT04152447	injuries requiring staged surgical fixation i.e. ex fix orif	Allergies or other skin conditions	Medical history
NCT03996954	patients unable unwilling use device	Medical history	Ability to provide informed consent

Search

DTx Clinical Trials

Upload custom file

Study options

Study Type(s)

Interventional Observational

Study Status

Completed Recruiting

Enrolling by invitati... Not yet recruiting Active, not recruiting

Study Timeframe

012 2030

2012 2030

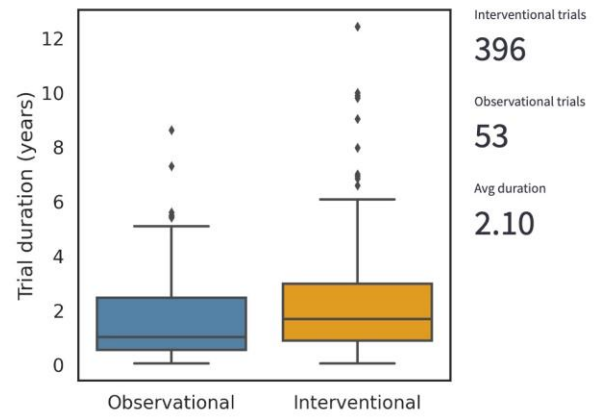
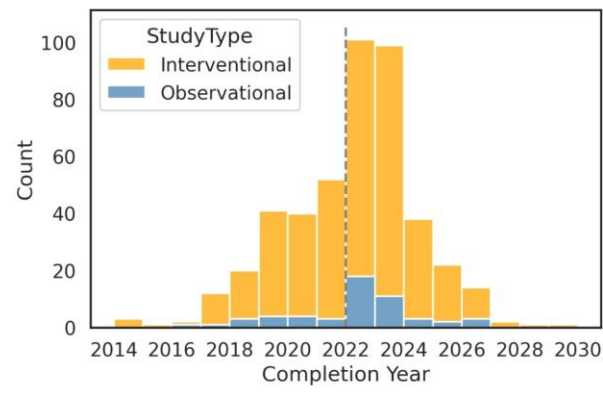
Limit to FDA regulated devices

Sponsor Types

INDUSTRY OTHER

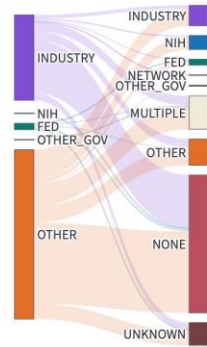
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Sponsor and collaborator metrics

Primary Sponsors & Collaborator Typ



Normalize to state population

Number of clinical trial locations by state

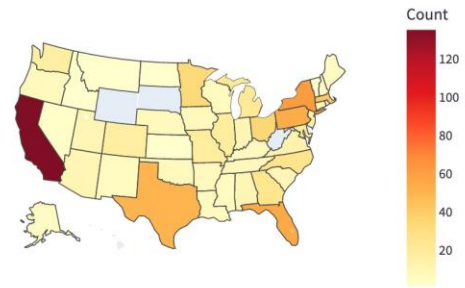


Figure S4. Clinical trials analysis dashboard. Screenshot of an interactive dashboard for analysis of ClinicalTrials.gov metadata for DTx clinical trials, provided for readers.