Pharmacovigilance in the Age of Legalized Cannabis: Using Social Media to Monitor Drug-Drug Interactions Between Immunosuppressants and Cannabis-Derived Products

Matthew R. Allen, B.S.[1,2], Gwenyth Portillo Wightman, M.S.E.[3], Zechariah Zhu, B.S.[2,4], Adam Poliak, Ph.D.[5], Davey M. Smith, M.D.[2,6], Mark Dredze, Ph.D.[3], John W. Ayers, Ph.D., M.A.[2,4,6]

[1] School of Medicine, University of California San Diego, La Jolla, California

[2] Altman Clinical and Translational Research Institute, University of California San Diego, La Jolla, California

[3] Department of Computer Science, Johns Hopkins University, Baltimore, Maryland

[4] Qualcomm Institute, University of California San Diego, La Jolla, California

[5] Department of Computer Science, Bryn Mawr College, Bryn Mawr, Pennsylvania

[6] Division of Infectious Diseases and Global Public Health, University of California San Diego, La Jolla, California

Corresponding Author: John W. Ayers, PhD MA; #333 CRSF 9500 Gilman Drive, La Jolla, California 92093; Phone: 619.371.1846; E-Mail: ayers.john.w@gmail.com; Website: www.johnwayers.com

Replication Instructions

The raw data must be obtained from Reddit due to their terms of use: https://www.reddit.com/r/reddit.com/wiki/api/ We provide instructions herein on how to rpelicate the procedures to generate out data.

First, we conducted a systematic search on Reddit to identify subreddits focused on either CDPs or health using 23 health-related and 137 CDP-related keywords **(Table S1)**. We identified 99 subreddits focused on CDP, 71 focused on health, and then downloaded all 63,561,233 associated posts made worldwide between the inception of Reddit on June 23, 2005 through December 31, 2021 **(Tables S2 and S3)**.

Second, we extracted posts from CDP-focused subreddits mentioning “tacrolimus” or related terms for alternative immunosuppressant drug names (i.e., “afinitor,” “afinitor disperz,” “astagraf,” “astagraf xl,” “cyclosporine,” “envarsus,” “envarsus xr,” “everolimus,” “fyarro,” “gengraf,” “hecoria,” “lupkynis,” “neoral,” “prograf,” “rapamune,” “rapamycin,” “sandimmune,” “sirolimus,” “voclosporin,” and “zortress”) or generic terms for immunosuppressants (e.g., “immunosuppressant(s)”). We also extracted posts from health subreddits that mentioned both one of the immunosuppressant keywords and CDPs (“cannabidiol,” “CBD,” “THC,” and “cannabis”) for further analysis.

Posts containing relevant keywords were reviewed by two blinded investigators (G.P.W., Z.Z.) who resolved any disagreements with a third investigator (J.W.A.) The evaluators were provided a working definition of adverse events defined as any undesirable clinically meaningful change in symptoms associated with the use of immunosuppressants and CDPs, shown the entire post, including title, and asked to answer two questions: 1) Did the post express concern about a

potential DDI involving consumer CDP and immunosuppressants (yes/no)? 2) Did the post describe a unique adverse event attributed to a DDI involving a consumer CDP and immunosuppressants (yes/no)? The annotated posts are available in the corresponding datafiles.

Table S1. Health and CDP related keywords used in subreddit identification.	
Keyword	**Number of Posts**
ambulance	health
doctor	health
doctors	health
emergency	health
emergency clinic	health
emergency room	health
emergency treatment	health
er	health
hospital	health
hospitalization	health
nurse	health
urgent care	health
clinic	health
diagnose	health
diagnosed	health
diagnosis	health
doctor's appointment	health
doctor's office	health
medicine	health
surgeon	health
surgery	health
treatment	health
called 911	health
cannabis	CDP
marihuana	CDP
marijuana	CDP
710	CDP

11 nor	CDP
11-nor	CDP
9 nor	CDP
9-nor	CDP
9b	CDP
acetate ester	CDP
athc	CDP
bhang	CDP
broad spectrum cbd	CDP
broad spectrum hemp	CDP
broad spectrum supplement	CDP
brownie	CDP
cannabichromene	CDP
cannabidiol	CDP
cannabidiolic	CDP
cannabidiolic acid	CDP
cannabidivarin	CDP
cannabigerol	CDP
cannabinoid	CDP
cannabinoids	CDP
cannabinol	CDP
cannabis essential oil	CDP
cannabis tea	CDP
cannabutter	CDP
cbc	CDP
cbd	CDP
cbd extract	CDP
cbd oil	CDP
cbda	CDP
cbdv	CDP
cbg	CDP
cbn	CDP

chara	CDP
d10 tetrahydrocannabinol	CDP
d10 thc	CDP
d10-tetrahydrocannabinol	CDP
d10-thc	CDP
d10thc	CDP
d8 tetrahydrocannabinol	CDP
d8 thc	CDP
d8-tetrahydrocannabinol	CDP
d8-thc	CDP
d8thc	CDP
d9 tetrahydrocannabinol	CDP
d9 thc	CDP
d9-tetrahydrocannabinol	CDP
d9-thc	CDP
d9thc	CDP
dab	CDP
dab rig	CDP
dabbed	CDP
dabbing	CDP
delta 10	CDP
delta 10 tetrahydrocannabinol	CDP
delta 10 thc	CDP
delta 8	CDP
delta 8 tetrahydrocannabinol	CDP
delta 8 thc	CDP
delta 9	CDP
delta 9 tetrahydrocannabinol	CDP
delta 9 thc	CDP
delta-10	CDP
delta-10 tetrahydrocannabinol	CDP
delta-10 thc	CDP

delta-10-tetrahydrocannabinol	CDP
delta-10-thc	CDP
delta-8	CDP
delta-8 tetrahydrocannabinol	CDP
delta-8 thc	CDP
delta-8-tetrahydrocannabinol	CDP
delta-8-thc	CDP
delta-9	CDP
delta-9 tetrahydrocannabinol	CDP
delta-9 thc	CDP
delta-9-tetrahydrocannabinol	CDP
delta-9-thc	CDP
delta10	CDP
delta10 tetrahydrocannabinol	CDP
delta10 thc	CDP
delta8	CDP
delta8 tetrahydrocannabinol	CDP
delta8 thc	CDP
delta9	CDP
delta9 tetrahydrocannabinol	CDP
delta9 thc	CDP
doobie	CDP
edible	CDP
edibles	CDP
extract	CDP
full spectrum cbd	CDP
full spectrum hemp	CDP
full spectrum supplement	CDP
gummies	CDP
gummy	CDP
hash oil	CDP
hashish	CDP

hemp extract	CDP
hemp juice	CDP
hemp oil	CDP
hhc	CDP
honey oil	CDP
hydroxyhexahydrocannabinol	CDP
kief	CDP
live resin	CDP
oil	CDP
oil rig	CDP
space cake	CDP
spliff	CDP
t h c	CDP
taffy	CDP
tea	CDP
tetrahydrocannabinol	CDP
tetrahydrocannabinolic	CDP
tetrahydrocannabinolic acid	CDP
tetrahydrocannabiphorol	CDP
tetrahydrocannabivarin	CDP
thc	CDP
thc 0	CDP
thc 0 acetate	CDP
thc acetate ester	CDP
thc-0	CDP
thc-0-acetate	CDP
thc0	CDP
thca	CDP
thcp	CDP
thcv	CDP
tincture of cannabis	CDP
vape	CDP

vape juice	CDP
vape oil	CDP
vaping	CDP
vaporizer	CDP
wax	CDP

Table S2. Number of posts on CDP-related subreddits through December 31, 2021.

Subreddit	Number of Posts
trees	27,929,696
microgrowery	3,818,781
weedstocks	3,007,909
weed	2,721,911
vaporents	2,122,737
leaves	1,148,914
oilpen	665,551
saplings	602,468
uktrees	598,659
cannabiscultivation	560,151
fakecartridges	557,071
delta8	551,936
entwives	450,420
canadients	445,158
treedibles	437,415
hempflowers	436,656
eldertrees	394,175
mflb	357,274
bostontrees	311,416
ausents	270,048
cannabis	186,752
puffco	173,497

outdoorgrowing	143,056
vegastrees	104,282
craftymighty	92,585
420	87,505
ploompax	83,372
chicagotrees	74,151
swedents	73,169
cleancarts	70,469
mainetrees	57,936
CannabisGrowers	43,474
cbdinfo	41,104
CannabisExtracts	37,834
armmj	36,958
arizer	34,799
CBD	33,746
medicalmarijuana	33,349
altcannabinoids	24,599
noids	22,838
puffitup	21,665
Cannabis_Culture	18,248
CanadianCannabisLPs	15,139
portabledabs	13,766
creamcityvapes	7,241
texasents	6,217
BoundlessVapes	4,601
davincivaporizer	4,487
AdvancedVapeSupply	4,022
cbg	3,434
healthyrips	3,417
electricents	992
vapor	977
magicflightlaunchbox	128

7thFloor	9
THC	2
Cannabidiol	1

Table S3. Number of posts on health-related subreddits through December 31, 2021.

Subreddit	Number of Posts
AskDocs	3,152,210
Health	1,485,209
mentalhealth	1,221,799
diabetes	977,633
Dentistry	942,187
birthcontrol	704,137
CrohnsDisease	641,223
ChronicPain	544,447
migraine	527,224
PCOS	466,778
cancer	382,624
MultipleSclerosis	370,673
cfs	254,597
insomnia	253,332
STD	235,363
GERD	220,542
benzorecovery	205,659
antidepressants	201,155
DiagnoseMe	163,579
Psoriasis	162,192
HealthInsurance	137,930
Allergies	136,905
rheumatoid	119,685
ChronicIllness	83,689

askdentists	82,290
scoliosis	75,059
Sciatica	75,013
dementia	70,274
breastcancer	61,194
obgyn	52,596
healthIT	44,672
Thritis	42,788
ClotSurvivors	42,160
FoodAllergies	40,293
lymphoma	39,779
transplant	38,586
dialysis	34,253
PsoriaticArthritis	31,416
pancreatitis	22,214
DSPD	22,067
braincancer	22,045
mastcelldisease	18,454
Urology	18,197
Constipation	17,632
menstruation	16,880
hearing	16,058
leukemia	13,193
Hypermobility	13,035
ATRIALFIBRILLATION	12,934
HiatalHernia	10,871
panicdisorder	9,695
Allergy	9,465
urticaria	8,476
AskHealth	8,368
askadentist	7,608
fibro	6,688

seizures	5,248
flu	5,075
multiplemyeloma	4,964
AskADoctor	3,871
Cirrhosis	3,810
AskaPharmacist	3,319
crazyitch	2,830
Ovariancancer	2,492
T1D	2,407
Antibiotics	1,567
hepc	1,521
Constipated	419
DuaneSyndrome	305
Colic	202
AskaDoc	11