

Electronic Supplementary Material 1

Article Title: Methods to compare Adverse Events in Twitter to FAERS, Drug Information Databases, and Systematic Reviews: Proof of Concept with Adalimumab

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Appendix 1

Appendix 1: Pooled Adverse Events mentioned in Micromedex, Lexicomp, and Clinical Pharmacology to Estimate Averages

Adverse Event Category	Micromedex	Lexicomp	Clinical Pharmacology	Drug Database Composite Average
Injection Site Reactions	Injection site reaction: Adult 8-20%; Injection site pain: Pediatric 6-19% Injection site reaction: Pediatric 5-16% Rash 12%	Injection site reaction: 12-20%, erythema, itching, hemorrhage, pain, swelling Rash 6-12%	Injection site reaction: Adult: 20% Injection site pain: Pediatric 6-19% Injection site reaction Pediatric: 5-16% Rash 12%	13.8%
Musculoskeletal: Fatigue; weakness, spasms, malaise (Creatinine kinase: surrogate marker)	Creatine kinase, Pediatric 15% Weakness associated with Guillane Barre: 1 case report	Muscle cramps <5% Increased creatinine phosphokinase: 15% Weakness <1% Guillane Barre <1% Myositis (Pediatric)<1%	Creatine phosphokinase Pediatric: 15% Muscle cramps <5% Myasthenia <5% Myositis Pediatric<5%	7%
Pain, all locations	Chest Pain <5% Abdominal pain 7% composite	Chest Pain <5% Torso pain <5% Abdominal pain 7% Pelvic Pain <5% Back pain 6% Limb pain <5%	Chest Pain <5% Abdominal Pain 7% Back pain 6% Extremity, pelvic, thorax pain all <5%	5.5%
Abdominal	Nausea 9% GI hemorrhage <5% Vomiting: 1 case report	Nausea 9%, cholecystitis 5%, cholelithiasis <5%, esophagitis <5%, gastrointestinal hemorrhage <5%, vomiting <5%	cholecystitis 5%, cholelithiasis <5%, esophagitis <5%, vomiting <5% GI Bleed/perforation <= 5%	7%
Neurologic symptoms: Anxiety/ Depression/ Isomnia/ Panic/ Mood disorders	Not reported	Confusion <5%	Confusion<5%	2.5%
Dermatologic	Rash 12% Psoriasis: case reports, rate not listed	Rash: 6-12% Plaque psoriasis: 3% Psoriasis: (new onset, palmoplantar, pustular, exacerbation) <1%	Rash: 12% Psoriasis: Rate not listed Pruritis: rate not listed	12%
Hypersensitivity	Hypersensitivity: Pediatric, 5-6% Adult: case report	Hypersensitivity: Pediatric 6%; Adult 1%	Hypersensitivity: Pediatric 6% Anaphylaxis 1% Nonspecific allergy in children <6%	1%

Infection	Sinusitis 11%, Upper respiratory 17% Influenza 7% Pneumonia, fungal, cellulitis, gastroenteritis: listed without rate Pediatric Infectious disease: 45% to 78%	Upper Respiratory 17% Sinusitis 11% Urinary Tract <8% "Serious Infection" 9% Pneumonia <4% Herpes simplex, zoster <4% Fungal <1% Cellulitis: 1-10%	Upper Respiratory 17% Sinusitis 11% Influenza 7% Urinary Tract 8% Gastroenteritis <5%	9.6% (Serious infection such as Tuberculosis examined separately)
Headache	Headache 12%	Headache: 12%	Headache 12%	12%
Neurologic: Dizzy-fall, gait, groggy, memory, confusion	Case report: gait disturbance	Confusion <5%	Confusion <5% Syncope <5% Tremor <5%	2.5%
Endocrine/metabolic	Hyperlipidemia 7%	Hyperlipidemia 7% Hypercholesterolemia 6% Dehydration <5% Ketosis <5%	Hyperlipidemia 7% Hypercholesterolemia 6% Dehydration <5% Ketosis <5%	4.5%
Arthralgia, joint pain, arthropathy, arthritis not related to condition	Arthralgia 3%	Arthralgia 3% Arthropathy <5% Arthritis <5%	Arthralgia 3%	3%
Cardiovascular	Atrial fibrillation <5%, Cardiac arrest <5%, Cardiac dysrhythmia <5%, Chest pain <5%, Heart failure, <5%, Myocardial infarction <5%, Palpitations <5%	Atrial fibrillation <5%, cardiac arrest <5%, cardiac arrhythmia <5%, chest pain <5%, coronary artery disease <5%, myocardial infarction <5%, palpitations <5%, tachycardia <5%	Cardiac arrest, pericardial effusion, pericarditis, and syncope <5%	2.5%
Hematologic/Oncologic	Thrombosis: case report Bleeding: case report Anemia: case report Leukopenia: case report In adult clinical trials, the most common reported malignancies were lymphoma, non-melanoma skin cancer, melanoma, and malignancies of the breast, colon, prostate, and lung Lymphoma: Package insert states 3 fold risk Melanoma: Package insert states risk, no rates reported Carcinoma: case report Prostate Cancer no rates reported Breast cancer no rates reported	All anemias <1% Neutropenia <1% Leukopenia <1% Thrombocytopenia <1% Deep vein thrombosis <5% Pulmonary embolism <1% Leukemia <1% Carcinomas: <1% Lymphomas: <1% Melanoma: no rates reported	Agranulocytosis <5% Subdural hematoma <5% leg thrombosis <5% polycythemia <5% Lymphomas: potential risk, no rate Non-melanoma skin cancer: 0.7/100 patient years (control rate 0.8/100 PY) Leukemia and carcinomas may have increased risk- no rates reported	1%

Hepatic	Liver enzyme elevations 4.4% Acute hepatic failure: case report Hepatic necrosis <5% Hepatitis: case report Hepatitis B reactivation: rate not listed	Increased liver enzymes 5% Hepatic necrosis <5% Hepatic failure <1% Hepatic necrosis <1% Hepatitis B reactivation: <1% Idiosyncratic hepatotoxicity <1%	Elevated liver enzymes 3.5% Elevated liver enzymes in pediatric patients: 2.6-4.4% Hepatic necrosis <5% Hepatitis B reactivation: rate not listed Acute liver failure and hepatitis: rate not reported	Composite 2.4%
Ophthalmic	Optic neuritis: case report	Cataract <5%	Cataract <5%	2.5%
Renal	Not reported	Nephrolithiasis <5%	Kidney Calculus <5%	2.5%
Respiratory	Bronchospasm <5% Dyspnea <5% Pleural effusion <5% Interstitial disease: rate not reported	Asthma <5% Bronchospasm <5% Dyspnea <5% Pleural effusion <5% Respiratory depression <5%	Dyspnea <5% Pulmonary fibrosis: rate not reported	2.5%

Serious: angioedema, in CP & faers face swelling

TB

Heart attack

Common: dermatologic greater than injection site due to 519 reports of psoriasis- in twitter we classified this as indication

Note: package insert has many updates, but not databases

See black box warning for malignancies

Lexicomp: Elderly: Infection and malignancy has been reported at a higher incidence; use caution in elderly patients.

If "<" was in range then center value was selected as point estimate; e.g. if categories were <1%, or <5% then 0.5% was selected as point estimate for <1 and 2.5% was selected for <5%

Unified Medical Language System Concept Codes and Adverse Reaction Categories

Category	umlsconceptnameKO	UMLS conceptIdKO
<u>Abdominal</u>	c0000729	abdominal cramp
	c0000737	abdominal pain
	c0009806	constipation
	c0392176	gi upset
	c0278061	hard stools
	c0235119	hunger abnormal
	c1258215	ileus
	c0232461	increase appetite
	c1971624	lack of appetite
	c0375548	nausea
	c0027497	nausea
	c0221512	pain stomach
	c0030252	palpitations
	c0344375	stomach cramps
	c0235309	stomach discomfort
	c0221512	stomach pain
	c0577027	stomach problem
	c0235309	stomach upset
	c0000731	swelling abdomen
	c0235309	upset stomach
c0042963	vomit	
c0018926	vomiting blood	
<u>Allergy</u>	c1527304	allergic reaction
	c0042109	hives
	c0151726	hypersensitivity injection site
Anxiety/Mood	c0278061	abnormal mental state
	c0001897	aggressive
	c0003467	anxiety
	c0700031	anxiety attack
	c0850592	feeling moody
	c0235129	feeling strange
	c0857486	felt like a zombie
	c0022107	irritable
	c0235109	mental distress

Neurologic/dizzy

c0085633	mood swings
c0746848	nerve problem
c0027769	nervous tension
c0027769	nervousness
c0086769	panic attacks
c0086796	panic attacks
c0038435	stress
c0038441	stress disorder
c0149784	stress reaction
c0541992	brain fog
c0009676	confusion
c0012833	dizzy
c0857087	dizzy spell
c0541992	groggy
c0220870	light-headed
c0751295	memory loss
c0442874	neuropathy
c0012833	wooziness
c0013144	drowsy
c0917799	excessive sleepiness
c0392674	exhausted
c0277794	extreme exhaustion
c0015672	fatigue
c0015672	lack of energy
c0023380	lethargic
c0015672	loss of energy
c0231218	malaise
c0235161	sleep decreased
c0037317	sleep disturbed
c0013144	sleepiness
c0234450	sleepy
c0015672	tired
c0239885	dull headache
c0221100	hangover effect
c0018681	headache
c0149931	migraine

Fatigue

Headache

Infection

c0000833 abscess
c0149725 chest infection
c0009443 common cold
c0149678 Epstein-barr virus infection
c0015967 fever
c0021400 flu
c0392171 flu-like symptoms
c0026946 fungal infection
c0021311 infection
c0947879 infection
c1609538 latent tuberculosis
c1609538 latent tuberculosis
c0032285 pneumonia
c1398341 sinus infection
c0522251 sinus pain
c0318712 viral gastroenteritis
c0042029 urinary tract infection

Injection Site

c0151698 injection site bleeding
c0521508 injection site bruising
c0877661 injection site burning
c0151734 injection site inflammation
c0852995 injection site itching
c0151775 injection site mass
c0151828 injection site pain
c0151735 injection site reaction
c1142080 injection site stinging
c0151605 injection site swelling
c0392196 injection site urticaria
c0033774 itch
c1096717 pain at the injection
c0521505 rash injection site

Myocardial/cardiac

c0549646 chest disorders
c0008031 chest pains
c0235239 heart fluttering
c0235239 heart irregular
c1868917 heart racing

Pain

c0030252	palpitations
c0234238	ache
c0239377	arm pain
c0151825	bone pain
c0016512	foot pain
c0019559	hip pain
c0003862	joint pain
c0231749	knee pain
c0023222	leg pain
c0231528	muscle pain
c0030193	pain
c0030794	pelvic pain
c0037011	shoulder pain
c0522251	sinus pain
c0231218	sick

Serious Illnesses that I would like to know separately:

c1609538	latent tuberculosis
c0019080	hemorrhage
c0206277	fatal outcome
c0149678	Epstein-barr virus infection