Modeling Path Importance for Effective Alzheimer's Disease Drug Repurposing (Supplementary Materials)

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S1. The Top-50 Drugs Identified by `MPI` and `BSL`

Table S1: Top-50 Drugs from `MPI`

Drug	MOA	Indication	Anti-`AD`	Evidence
varenicline	`AChR-Ag`	smoking cessation	N	-
fosinopril	`ACE-INH`	hypertension	Y	*in vivo*[1]
nicotine	`AChR-Ag`	smoking cessation	Y	clinical[2]
nizatidine	histamine receptor antagonist	duodenal ulcer disease	N	-
piroxicam	`COX-INH`	osteoarthritis	Y	other[3,4]
meloxicam	`COX-INH`	osteoarthritis	Y	*in vivo*[5–7]
galantamine	`AChE-INH`	Alzheimer's disease	Y	approved
bromfenac	`COX-INH`	inflammation	N	-
etodolac	`COX-INH`	osteoarthritis	Y	*in vivo*[8]
pyridostigmine	`AChE-INH`	myasthenia gravis	N	-
bupropion	dopamine reuptake inhibitor	depression	N	-
pentoxifylline	phosphodiesterase inhibitor	claudication	N	-
flurbiprofen	`COX-INH`	rheumatoid arthritis	Y	clinical[9]
zonisamide	sodium channel blocker	seizures	N	-
apixaban	coagulation factor inhibitor	stroke	Y	other[3,4]
rivastigmine	`AChE-INH`	Alzheimer's disease	Y	approved
ramipril	`ACE-INH`	hypertension	Y	clinical[10]
linezolid	bacterial 50S ribosomal subunit inhibitor	pneumonia	N	-
trandolapril	`ACE-INH`	hypertension	Y	*in vivo*[11]
moexipril	`ACE-INH`	hypertension	N	-
quinapril	`ACE-INH`	hypertension	N	-

Drug	MOA	Indication	Anti-AD	Evidence
enalapril	ACE-INH	hypertension	N	-
benazepril	ACE-INH	hypertension	N	-
lisinopril	ACE-INH	hypertension	Y	*in vivo*[12]
hydralazine	vasodilator	hypertension	Y	*in vitro*[13]
rasagiline	monoamine oxidase inhibitor	Parkinson's Disease	Y	clinical[14]
ganciclovir	DNA polymerase inhibitor	cytomegalovirus	Y	*in vivo*[15]
naproxen	COX-INH	pain relief	N	-
fluvoxamine	selective serotonin reuptake inhibitor	obsessive compulsive disorder	Y	*in vivo*[16]
dapsone	bacterial antifolate	dermatitis herpetiformis	Y	other[17]
oxaprozin	COX-INH	osteoarthritis	Y	other[3,4]
ranitidine	histamine receptor antagonist	heartburn	N	-
donepezil	AChE-INH	Alzheimer's disease	Y	approved
memantine	glutamate receptor antagonist	Alzheimer's disease	Y	approved
empagliflozin	sodium/glucose cotransporter inhibitor	diabetes mellitus	Y	*in vivo*[18]
canagliflozin	sodium/glucose cotransporter inhibitor	diabetes mellitus	N	-
alogliptin	dipeptidyl peptidase inhibitor	diabetes mellitus	Y	*in vivo*[19,20]
oxiconazole	bacterial cell wall synthesis inhibitor	tinea pedis	N	-
rivaroxaban	coagulation factor inhibitor	stroke	Y	*in vivo*[21]
fluoxetine	selective serotonin reuptake inhibitor	depression	Y	*in vivo*[22]
azelastine	histamine receptor antagonist	conjunctivitis	N	-
sertraline	selective serotonin reuptake inhibitor	depression	N	-
ibuprofen	COX-INH	headache	N	-
labetalol	adrenergic receptor antagonist	hypertension	N	-
duloxetine	norepinephrine reuptake inhibitor	depression	N	-
quinine	hemozoin biocrystallization inhibitor	malaria	N	-
trihexyphenidyl	acetylcholine receptor antagonist	parkinsonism	N	-
ketoprofen	COX-INH	rheumatoid arthritis	N	-
selegiline	monoamine oxidase inhibitor	Parkinson's Disease	N	-
nortriptyline	tricyclic antidepressant	depression	N	-

In this table, the column "Drug" shows the identified top-50 ranked drugs; the column "MOA" shows the mechanism of action of each drug; the column "Indication" presents the indication of each drug; the column "Anti-AD " indicates if the drug has evidenced anti-AD effects; and the column "Evidence" presents the type of the evidence. In this table, ACE-INH represents the angiotensin converting enzyme inhibitor; COX-INH represents the cyclooxygenase inhibitor; AChE-INH represents the acetylcholinesterase inhibitor; and AChR-Ag represents the acetylcholine receptor agonist.

Table S2: Top-50 Drugs from `BSL`

Drug	MOA	Indication	Anti-`AD`	Evidence
tetracycline	bacterial 30S ribosomal subunit inhibitor	respiratory tract infections	Y	*in vitro*[23]
selegiline	monoamine oxidase inhibitor	Parkinson's Disease	N	-
ceftriaxone	bacterial cell wall synthesis inhibitor	gonorrhea	Y	*in vivo*[24]
ibuprofen	`COX-INH`	headache	N	-
levobunolol	adrenergic receptor antagonist	glaucoma	N	-
ketoprofen	`COX-INH`	rheumatoid arthritis	N	-
carbidopa	aromatic L-amino acid decarboxylase inhibitor	Parkinson's Disease	N	-
sulindac	`COX-INH`	osteoarthritis	Y	*in vivo*[25]
biotin	vitamin B	supplement	Y	*in vivo*[26]
lansoprazole	ATPase inhibitor	heartburn	N	-
itraconazole	cytochrome P450 inhibitor	onychomycosis	N	-
ketorolac	`COX-INH`	pain relief	N	-
quinidine	sodium channel blocker	malaria	N	-
terbinafine	fungal squalene epoxidase inhibitor	tinea pedis	N	-
labetalol	adrenergic receptor antagonist	hypertension	N	-
vilazodone	serotonin reuptake inhibitor	depression	N	-
ivermectin	benzodiazepine receptor agonist	gastrointestinal roundworms	N	-
oxiconazole	bacterial cell wall synthesis inhibitor	tinea pedis	N	-
dabigatran	thrombin inhibitor	stroke	Y	*in vivo*[27]
linezolid	bacterial 50S ribosomal subunit inhibitor	pneumonia	N	-
indomethacin	`COX-INH`	rheumatoid arthritis	Y	clinical[28]
donepezil	`AChE-INH`	Alzheimer's disease	Y	approved
levodopa	dopamine precursor	Parkinson's Disease	N	-
ketoconazole	sterol demethylase inhibitor	seborrheic dermatitis	N	-
loratadine	histamine receptor antagonist	allergic rhinitis	N	-
lovastatin	HMGCR inhibitor	coronary heart disease	Y	other[29]
triamterene	sodium channel blocker	hypokalemia	Y	clinical[30]
captopril	`ACE-INH`	hypertension	Y	*in vivo*[31]
naproxen	`COX-INH`	pain relief	N	-
methyldopa	adrenergic receptor agonist	hypertension	N	-
fluvoxamine	selective serotonin reuptake inhibitor	obsessive compulsive disorder	Y	*in vivo*[16]
zonisamide	sodium channel blocker	seizures	N	-
diflunisal	prostanoid receptor antagonist	rheumatoid arthritis	Y	*in vivo*[32]
sertraline	selective serotonin reuptake inhibitor	depression	N	-
rasagiline	monoamine oxidase inhibitor	Parkinson's Disease	Y	clinical[14]
verapamil	calcium channel blocker	hypertension	Y	*in vivo*[33]
metoclopramide	dopamine receptor antagonist	gastroparesis	N	-

diclofenac	COX-INH	rheumatoid arthritis	Y	other[34]
bupropion	dopamine reuptake inhibitor	depression	N	-
amiloride	sodium channel blocker	hypertension	Y	clinical[30]
vortioxetine	serotonin receptor agonist	depression	N	-
trazodone	adrenergic receptor antagonist	depression	N	-
losartan	angiotensin receptor antagonist	hypertension	N	-
trihexyphenidyl	acetylcholine receptor antagonist	parkinsonism	N	-
fluoxetine	selective serotonin reuptake inhibitor	depression	Y	*in vivo*[22]
azelastine	histamine receptor antagonist	conjunctivitis	N	-
nicotine	AChR-Ag	smoking cessation	Y	clinical[2]
dexamethasone	glucocorticoid receptor agonist	hypercalcemia	Y	*in vivo*[35]
doxazosin	adrenergic receptor antagonist	benign prostatic hyperplasia	Y	*in vitro*[36]
tramadol	centrally-acting opioid agonist	pain management	N	-

These columns have the same meaning as those in Table S1.

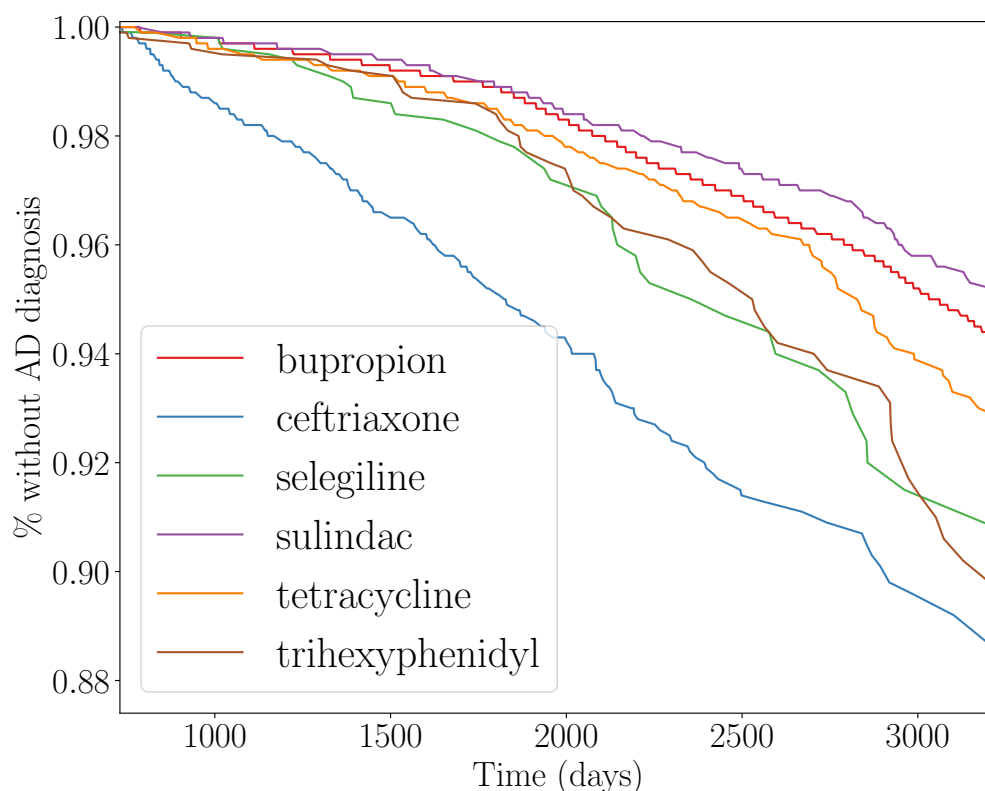## S2. BSL Survival Analysis

Fig. S1: Unadjusted Kaplan−Meier plots for BSL's top-ranked evidential drugs.

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