

Supplementary material 1

Journal: Clinical Pharmacokinetics

Physiologically Based Pharmacokinetic (PBPK) Modeling of Antidepressants: A Scoping Review of existing models, applications, and software-tools

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Supplementary File 1: Search strategy

A comprehensive search strategy combining controlled vocabulary (e.g. Mesh and Emtree terms) and free-text keywords was developed to identify relevant studies. The selection of search terms was guided by the key concepts of this scoping review. Search strings were iteratively refined to ensure adequate sensitivity and specificity.

The strategy was designed to capture two main concepts central to this review:

1. physiologically based pharmacokinetic (PBPK) modeling
2. antidepressant drugs

Search terms were combined using Boolean operators and adapted for each database.

PubMed

Search was conducted on July 19, 2025, at 9:23

Number of records: 481

Concept	Search	Results
1	"pharmacokinetic model*" [tiab] OR "in silico pharmacokinetic*" [tiab] OR PBPK [tiab] OR PBK [tiab] OR PBTK [tiab] OR "physiologically based pharmacokinetic*" [tiab] OR "physiologically based kinetic*" [tiab] OR "physiologically based toxicokinetic*" [tiab] OR "physiologically based model*" [tiab] OR "PK-SIM" [tiab] OR SimCyp [tiab] OR Mobi [tiab] OR GastroPlus [tiab]	16,468
2	("Antidepressive Agents" [mesh] OR antidepressant* [tiab] OR "selective serotonin reuptake inhibitors" [mesh] OR "Serotonin and Noradrenaline Reuptake Inhibitors" [mesh] OR "Monoamine Oxidase Inhibitors" [mesh] OR "mental disorders" [mesh] OR Citalopram [tiab] OR Escitalopram [tiab] OR Fluoxetine [tiab] OR Fluvoxamine [tiab] OR Paroxetine [tiab] OR Sertraline [tiab] OR Venlafaxine [tiab] OR Desvenlafaxine [tiab] OR Duloxetine [tiab] OR Milnacipran [tiab] OR Amitriptyline [tiab] OR Clomipramine [tiab] OR Doxepin [tiab] OR Imipramine [tiab] OR Nortriptyline [tiab] OR Trimipramine [tiab] OR Opipramol [tiab] OR Mirtazapine [tiab] OR Mianserin [tiab] OR Moclobemide [tiab] OR Tranylcypromine [tiab] OR Bupropion [tiab] OR Agomelatine [tiab] OR Tianeptine [tiab] OR Trazodone [tiab] OR psychiatr* [tiab] OR psychiatry [mesh] OR Citalopram [mesh] OR Escitalopram [mesh] OR Fluoxetine [mesh] OR Fluvoxamine [mesh] OR Paroxetine [mesh] OR Sertraline [mesh] OR "Venlafaxine Hydrochloride" [mesh] OR "Desvenlafaxine succinate" [mesh] OR "Duloxetine Hydrochloride" [mesh] OR Milnacipran [mesh] OR Amitriptyline [mesh] OR Clomipramine [mesh] OR Doxepin [mesh] OR Imipramine [mesh] OR Nortriptyline [mesh] OR Trimipramine [mesh] OR Opipramol [mesh] OR Mirtazapine [mesh] OR Mianserin [mesh] OR Moclobemide [mesh] OR Tranylcypromine [mesh] OR Bupropion [mesh] OR Agomelatine [supplementary concept] OR Tianeptine [supplementary concept] OR Trazodone [mesh] OR Reboxetine [mesh] OR Reboxetine [tiab] OR Esketamine [supplementary concept] OR Esketamine [tiab])	1,842,980
1 + 2		481

Search was conducted on July 19, 2025, at 9:09
Number of record: 60

PBPk Antidepressant V4			
Last saved on: 19/07/2025 09:00:03			
✔ Search saved.			
		New filter (0) Print search history	
+ +	#1	(PBPk)1,ab,ba	S* Limits 95
+ +	#2	(PBPk)1,ab,ba	S* Limits 20
+ +	#3	(PBPk)1,ab,ba	S* Limits 3
+ +	#4	(glyxylglycylglycyl N-oxyl) based N-oxyl known*)1,ab,ba	S* Limits 0
+ +	#5	(glyxylglycylglycyl N-oxyl) based N-oxyl pharmacokinetic*)1,ab,ba	S* Limits 92
+ +	#6	(glyxylglycylglycyl N-oxyl) based N-oxyl model*)1,ab,ba	S* Limits 11
+ +	#7	(pharmacokinetic N-oxyl model*)1,ab,ba	S* Limits 1341
+ +	#8	(in N-oxyl N-oxyl N-oxyl pharmacokinetic*)1,ab,ba	S* Limits 2
+ +	#9	(glyxylglycylglycyl N-oxyl) based N-oxyl pharmacokinetic*)1,ab,ba	S* Limits 1
+ +	#10	(N-oxyl N-oxyl)1,ab,ba	S* Limits 4
+ +	#11	(MeSH)1,ab,ba	S* Limits 86
+ +	#12	(MeSH)1,ab,ba	S* Limits 33
+ +	#13	(MeSH)1,ab,ba	S* Limits 14
+ +	#14	MeSH descriptor: [Antidepressant Agents] explode all trees	MeSH+ 7596
+ +	#15	(antidepressant*)1,ab,ba	S* Limits 16373
+ +	#16	MeSH descriptor: [Selective Serotonin Reuptake Inhibitors] explode all trees	MeSH+ 3498
+ +	#17	MeSH descriptor: [Serotonin and Noradrenaline Reuptake Inhibitors] explode all trees	MeSH+ 86
+ +	#18	MeSH descriptor: [Monoamine Oxidase Inhibitors] explode all trees	MeSH+ 423
+ +	#19	MeSH descriptor: [Monoamine Oxidase Inhibitors] explode all trees	MeSH+ 110917
+ +	#20	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1768
+ +	#21	(tricyclic)1,ab,ba	S* Limits 2796
+ +	#22	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 153
+ +	#23	(tricyclic)1,ab,ba	S* Limits 2226
+ +	#24	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1720
+ +	#25	(tricyclic)1,ab,ba	S* Limits 3860
+ +	#26	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 483
+ +	#27	(tricyclic)1,ab,ba	S* Limits 1008
+ +	#28	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1141
+ +	#29	(tricyclic)1,ab,ba	S* Limits 2701
+ +	#30	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1258
+ +	#31	(tricyclic)1,ab,ba	S* Limits 2957
+ +	#32	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 825
+ +	#33	(tricyclic)1,ab,ba	S* Limits 2006
+ +	#34	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 154
+ +	#35	(tricyclic)1,ab,ba	S* Limits 288
+ +	#36	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 778
+ +	#37	(tricyclic)1,ab,ba	S* Limits 1852
+ +	#38	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 154
+ +	#39	(tricyclic)1,ab,ba	S* Limits 322
+ +	#40	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1377
+ +	#41	(tricyclic)1,ab,ba	S* Limits 2778
+ +	#42	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 473
+ +	#43	(tricyclic)1,ab,ba	S* Limits 953
+ +	#44	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 135
+ +	#45	(tricyclic)1,ab,ba	S* Limits 465
+ +	#46	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1172
+ +	#47	(tricyclic)1,ab,ba	S* Limits 2078
+ +	#48	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 509
+ +	#49	(tricyclic)1,ab,ba	S* Limits 938
+ +	#50	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 69
+ +	#51	(tricyclic)1,ab,ba	S* Limits 141
+ +	#52	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 26
+ +	#53	(tricyclic)1,ab,ba	S* Limits 40
+ +	#54	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 361
+ +	#55	(tricyclic)1,ab,ba	S* Limits 1837
+ +	#56	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 495
+ +	#57	(tricyclic)1,ab,ba	S* Limits 687
+ +	#58	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 208
+ +	#59	(tricyclic)1,ab,ba	S* Limits 370
+ +	#60	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 92
+ +	#61	(tricyclic)1,ab,ba	S* Limits 128
+ +	#62	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 1635
+ +	#63	(tricyclic)1,ab,ba	S* Limits 1975
+ +	#64	(tricyclic)1,ab,ba	S* Limits 374
+ +	#65	(tricyclic)1,ab,ba	S* Limits 142
+ +	#66	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 286
+ +	#67	(tricyclic)1,ab,ba	S* Limits 947
+ +	#68	(tricyclic)1,ab,ba	S* Limits 370
+ +	#69	MeSH descriptor: [Tricyclic Antidepressants] explode all trees	MeSH+ 202
+ +	#70	(tricyclic)1,ab,ba	S* Limits 1689
+ +	#71	(tricyclic)1,ab,ba	S* Limits 3861
+ +	#72	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	Limits 1443
+ +	#73	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	Limits 15279
+ +	#74	#12 AND #73	Limits 60
+ +	#75	Type a search term or use the 0 to 10 filters buttons to compare	S* MeSH+ Limits N/A
✖ Clear all ☐ Highlight orphan lines			

Embase (via Ovid)

Search was conducted on July 19, 2025, at 8:30

Number of records: 1456

- 1 ('pharmacokinetic model*' or 'in silico pharmacokinetic*' or pbpk or pbk or pbtk or 'physiologically based pharmacokinetic*' or 'physiologically based kinetic*' or 'physiologically based toxicokinetic*' or 'physiologically based model*' or pk-sim or simcyp or mobi or gastroplus).ti,ab. 20172
- 2 pharmacokinetic modeling software/ 2921
- 3 ('antidepressant*' or psychiatr* or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or venlafaxine or desvenlafaxine or duloxetine or milnacipran or amitriptyline or clomipramine or doxepin or imipramine or nortriptyline or trimipramine or opipramol or mirtazapine or mianserin or moclobemide or tranylcypromine or bupropion or agomelatine or tianeptine or trazodone or reboxetine or esketamine).ti,ab. 528863
- 4 exp antidepressant agent/ or exp mental disease/ or exp psychiatry/ 3204263
- 5 1 or 2 22007
- 6 3 or 4 3274514
- 7 5 and 6 1456

Search History (7) ^

☐	# ▲ Searches	Results
☐	1 ('pharmacokinetic model*' or 'in silico pharmacokinetic*' or pbpk or pbk or pbtk or 'physiologically based pharmacokinetic*' or 'physiologically based kinetic*' or 'physiologically based toxicokinetic*' or 'physiologically based model*' or pk-sim or simcyp or mobi or gastroplus).ti,ab.	20172
☐	2 pharmacokinetic modeling software/	2921
☐	3 ('antidepressant*' or psychiatr* or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or venlafaxine or desvenlafaxine or duloxetine or milnacipran or amitriptyline or clomipramine or doxepin or imipramine or nortriptyline or trimipramine or opipramol or mirtazapine or mianserin or moclobemide or tranylcypromine or bupropion or agomelatine or tianeptine or trazodone or reboxetine or esketamine).ti,ab.	528863
☐	4 exp antidepressant agent/ or exp mental disease/ or exp psychiatry/	3204263
☐	5 1 or 2	22007
☐	6 3 or 4	3274514
☐	7 5 and 6	1456

Web of Science

Search was conducted on July 19, 2025, at 10:13

Number of records: 452

TS=("pharmacokinetic model*" OR "in silico pharmacokinetic*" OR PBPK OR PBK OR PBTK OR "physiologically based pharmacokinetic*" OR "physiologically based kinetic*" OR "physiologically based toxicokinetic*" OR "physiologically based model*" OR "PK-SIM" OR SimCyp OR Mobi OR GastroPlus)

AND

TS=(antidepress* OR "serotonin reuptake inhibitor*" OR "serotonin uptake inhibitor*" OR SSRI* OR "Noradrenaline Reuptake Inhibitor*" OR "Noradrenaline uptake Inhibitor*" OR SNRI* OR NRI* OR "Monoamine Oxidase Inhibitor*" OR MAOI* OR "TCA*" OR "mental disorder*" OR depression OR Citalopram OR Escitalopram OR Fluoxetine OR Fluvoxamine OR Paroxetine OR Sertraline OR Venlafaxine OR Desvenlafaxine OR Duloxetine OR Milnacipran OR Amitriptyline OR Clomipramine OR Doxepin OR Imipramine OR Nortriptyline OR Trimipramine OR Opipramol OR Mirtazapine OR Mianserin OR Moclobemide OR Tranylcypromine OR Bupropion OR Agomelatine OR Tianeptine OR Trazodone OR psychiatr* OR Reboxetine OR Esketamine)

ClinicalTrials.gov

Search was conducted on July 19, 2025, at 12:04

Number of records: 36

("pharmacokinetic model" OR "pharmacokinetic models" OR "pharmacokinetic modeling" OR "pharmacokinetic modelling" OR "in silico pharmacokinetic" OR "in silico pharmacokinetics" OR PBPK OR PBK OR PBTK OR "physiologically based pharmacokinetic" OR "physiologically based pharmacokinetics" OR "physiologically based kinetic" OR "physiologically based kinetics" OR "physiologically based toxicokinetic" OR "physiologically based toxicokinetics" OR "physiologically based model" OR "physiologically based models" OR "physiologically based modeling" OR "physiologically based modelling" OR "PK-SIM" OR SimCyp OR Mobi OR GastroPlus)

AND

(antidepress* OR "serotonin reuptake inhibitor" OR "serotonin reuptake inhibitors" OR "serotonin uptake inhibitor" OR "serotonin uptake inhibitors" OR SSRI* OR "Noradrenaline Reuptake Inhibitor" OR "Noradrenaline Reuptake Inhibitors" OR "Noradrenaline uptake Inhibitor" OR "Noradrenaline uptake Inhibitors" OR SNRI* OR NRI* OR "Monoamine Oxidase Inhibitor" OR "Monoamine Oxidase Inhibitors" OR MAOI* OR "TCA*" OR "mental disorder" OR "mental disorders" OR depression OR Citalopram OR Escitalopram OR Fluoxetine OR

Fluvoxamine OR Paroxetine OR Sertraline OR Venlafaxine OR Desvenlafaxine OR Duloxetine
OR Milnacipran OR Amitriptyline OR Clomipramine OR Doxepin OR Imipramine OR
Nortriptyline OR Trimipramine OR Opipramol OR Mirtazapine OR Mianserin OR
Moclobemide OR Tranylcypromine OR Bupropion OR Agomelatine OR Tianeptine OR
Trazodone OR psychiatr* OR Reboxetine OR Esketamine)

PubPharm

Search was conducted on July 19, 2025, at 13:45

Number of records: 322

("PBPK" OR "physiologically based pharmacokinetic" OR "physiologically based
pharmacokinetics" OR "pharmacokinetic model" OR "pharmacokinetic models" OR
"pharmacokinetic modeling" OR "PBK") AND (antidepressant* OR "antidepressive agents"
OR "antidepressant therapy" OR "antidepressive treatment" OR "antidepressant drug")

OSP-based-publications-and-content (via GitHub)

Search was conducted on July 19, 2025, at 16:30

Number of records: 16

Sources of evidence	Search strategy	Number of records
Journals, Slides (presentation and poster), Models	Manual search by screening labels using the names of all included antidepressants and the terms “antidepressant,” “psych,” and “mental”	16