

Drug-drug Interaction between Psychotropic Medications and Medications Used in COVID-19: Comparison of Online Databases

Surobhi Chatterjee, Sujita Kumar Kar, Aathira Jaya Prakash, Teena Bansal, Garima Singh

Department of Psychiatry, King George's Medical University, Lucknow, Uttar Pradesh, India

Objective: COVID-19 has gravely affected patients with psychiatric conditions. Potential interactions may occur between psychotropic medications and medications used in treatment of COVID-19. This study aimed to compare the online databases in terms of the quality of drug-drug interaction related information available on them.

Methods: 216 drug interactions which included fifty-four psychotropic medication interactions with four COVID-19 drugs across six databases were analyzed by four authors independently. The overall grading of the databases was done on Likert scale independently by the authors using the parameters of ease of understanding for consumers and professionals, level of completeness, discussion on level of evidence and the number of available drugs, congruity with other databases and the mean score was tabulated.

Results: Drugbank and Lexicomp had maximum discrepancy. The safety profile of Hydroxychloroquine was the best (eighteen moderate/severe psychotropic medication reactions) while Ritonavir has worst profile with thirty-nine medications. Drugbank had the highest SCOPE score (1.00) for completeness and covid19druginteractions.com had least (0.81). Overall, Liverpool[®] Drug Interaction Group and Lexicomp scored the highest (23/30 each) and were the best interaction checker software closely followed by Drugs.com (22/30). Medscape and WebMD were the poorest interaction checker databases.

Conclusion: There is significant variability in the available online databases. Liverpool[®] Drug Interaction Group and Lexicomp were the most reliable sources for healthcare workers whereas for patients, Drugs.com was the easiest to understand (as it segregates the needs of general consumers and professionals distinctly to explain the interaction).

KEY WORDS: Drug-related side effects; Adverse reactions; Psychotropic drugs; COVID-19.

INTRODUCTION

Knowledge of drug-drug interaction is highly essential for safe clinical practice of medicine. Poor understanding about drug-drug interaction may result in development of significant adverse drug reactions, treatment failure, and poor adherence to treatment [1]. Patients with multiple medical morbidities are often prescribed with different groups of medication, which may have potential drug-drug interactions. Patients with psychiatric illnesses are at increased risk of medical morbidities and many such patients have multiple medical morbidities, which increases

the possibility of serious drug-drug interactions, if appropriate medications are not considered in combination.

Drug-drug interaction results from the pharmacokinetic changes. The pharmacokinetic changes result in increased therapeutic level of the drugs leading to development of adverse drug reactions or it may result in increased metabolism of a drug leading to decreased therapeutic level and hence inadequate response to the drug [2]. Psychotropic medications are known to have significant interaction with several medications including those used in the management of COVID-19.

Most of the textbooks and other scientific literature discuss the potential drug-drug interactions broadly but they are deficient in discussing the one-to-one interaction between the pharmacological agents and are neither frequently updated and nor freely accessible. This results in the usage of easily accessible online databases, that provides the details on potential drug-drug interactions and

Received: August 25, 2022 / **Revised:** October 23, 2022

Accepted: November 15, 2022

Address for correspondence: Sujita Kumar Kar

Department of Psychiatry, King George's Medical University,
Lucknow 226003, Uttar Pradesh, India

E-mail: drsujita@gmail.com

ORCID: <https://orcid.org/0000-0003-1107-3021>

© This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Table 1. Interaction of psychotropic medications with medications used in COVID-19 patients

Psychotropic medication	Congruity between different databases	Congruity in positive interaction (%)	Medscape	WebMD	Drugs.com	Drugbank	Lexicomp	Liverpool COVID-19 interactions
Escitalopram	5/6 (++++), 1/6 (+++)	HCA (6/6)-100% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(-)	H(+), C(+), A(+), R(+)
Sertraline	3/6 (++++), 2/6 (++++), 1/6 (---+)	H (5/6)-83.33% C (5/6)-83.33% A (4/6)-66.67% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)	H(+), C(+), A(+), R(-)	H(-), C(-), A(-), R(+)
Paroxetine	1/6 (++++), 4/6 (++++), 1/6 (+)	H (3/6)-50% C (5/6)-83.33% A (3/6)-50% R (6/6)-100%	H(-), C(+), A(+), R(+)	H(-), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)	H(+), C(+), A(-), R(+)
Fluoxetine	4/6 (++++), 2/6 (+++)	H (6/6)-100% C (6/6)-100% A (5/6)-83.33% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(-)	H(+), C(+), A(-), R(+)
Fluvoxamine	2/6 (+++), 1/6 (++), 3/6 (+)	H (3/6)-50% C (3/6)-50% A (1/6)-16.33% R (4/6)-66.66%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(-)	H(+), C(+), A(-), R(-)	H(+), C(+), A(-), R(+)
Citalopram	5/6 (++++), 1/6 (+++)	H (6/6)-100% C (6/6)-100% A (6/6)-100% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(-)	H(+), C(+), A(+), R(+)
Vortioxetine	1/6 (++++), 1/6 (++), 3/6 (+), 1/6 (----)	H (2/6)-33.33% C (2/6)-33.33% A (1/6)-16.33% R (4/6)-66.66%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(-)	H(-), C(-), A(-), R(-)
Duloxetine	1/6 (++++), 1/6 (++++), 2/6 (++), 2/6 (----)	H (2/6)-33.33% C (4/6)-66.66% A (1/6)-16.66% R (4/6)-66.66%	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(+), C(+), A(-), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)
Venlafaxine	3/6 (++++), 2/6 (++), 1/6 (----)	H (3/6)-50% C (3/6)-50% A (5/6)-83.33% R (5/6)-83.33%	H(-), C(-), A(+), R(+)	H(-), C(-), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(+), C(+), A(+), R(+)
Desvenlafaxine	1/6 (+++), 1/6 (++), 2/6 (+), 1/6 (----), 1/6-UN	H (5/6, UN)-83.33% C (2/6, UN)-33.33% A (1/6, UN)-16.66% R (4/6, UN)-66.67%	H(-), C(+), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(-)	H(-), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H, C, A, R
Mirtazapine	2/6 (++++), 1/6 (+++), 3/6 (+)	H (3/6)-50% C (3/6)-50% A (3/6)-50% R (5/6)-83.33%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(+), C(-), A(-), R(-)	H(+), C(+), A(+), R(+)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Bupropion	4/6 (++), 1/6 (+), 1/6 (----)	H (0/6)-0% C (3/6)-50% A (0/6)-0% R (5/6)-83.33%	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(-)
Tranlycypromine	1/6 (++), 5/6 (----)	H (1/6)-16.67% C (1/6)-16.67% A (0/6)-0% R (0/6)-0%	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(+), C(+), A(-), R(-)	H(-), C(-), A(-), R(-)

Table 1. Continued 1

Psychotropic medication	Congruity between different databases	Congruity in positive interaction (%)	Medscape	WebMD	Drugs.com	Drugbank	Lexicomp	Liverpool COVID-19 interactions
Imipramine	3/6 (++++), 2/6 (+++), 1/6 (+)	H (3/6)-50% C (5/6)-83.33% A (5/6)-83.33% R (6/6)-100%	H(-), C(+), A(+), R(+)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)
Clomipramine	5/6 (++++), 1/6 (+)	H (5/6)-83.33% C (5/6)-83.33% A (5/6)-83.33% R (6/6)-100%	H (+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)
Amitriptyline	5/6 (++++), 1/6 (+++)	H (5/6)-83.33% C (6/6)-100% A (6/6)-100% R (6/6)-100%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Nortriptyline	4/6 (++++), 1/6 (+++), 1/6 (----)	H (4/6)-66.67% C (5/6)-83.33% A (4/6)-66.67% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Trazodone	2/6 (++++), 2/6 (+++), 1/6 (++)	H (3/6)-50% C (4/6)-66.67% A (5/6)-83.33% R(6/6)-100%	H(-), C(-), A(+), R(+)	H(-), C(-), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Dosulepin	1/6 (++++), 1/6 (+), 1/6 (----), 3/6-UN	H (1/6, 2 UN)-16.67% (1/6, 2 UN)-16.67% A(1/6, 2 UN)-16.67% R(2/6, 2 UN)-33.33%	H(-), C(-), A(-), R(-)	H, C, A, R	H, C, A, R	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H, C, A, R
Agomelatine	2/6 (+), 1/6 (----), 3/6-UN	H (0/6, 3 UN)-0% C (0/6, 3 UN)-0% A (0/6, 3 UN)-0% R (1/6, 3 UN)-16.67%	H, C, A, R	H, C, A, R	H, C, A, R	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(+)
Tianeptine	1/6 (+++), 1/6 (+), 1/6 (----), 3/6-UN	H (0/6, 3 UN)-0% C (0/6, 3 UN)-0% A (1/6, 3 UN)-16.67% R (2/6, 3 UN)-16.67%	H, C, A, R	H, C, A, R	H, C, A, R	H(-), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(+)
Clozapine	6/6 (++++)	HCAR (6/6)-100%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Olanzapine	5/6 (++++), 1/6 (+)	H(5/6)-83.33% C(5/6)-83.33% A(5/6)-83.33% R(6/6)-100%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)
Risperidone	4/6 (++++), 2/6 (+++)	HCR (6/6)-100% A (4/6)-66.67%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)
Amisulpride	3/6 (++++), 1/6 (+++), 1/6 (----), 1/6-UN	H (4/6, 1 UN)-66.67% C (4/6, 1 UN)-66.67% A (4/6, 1 UN)-66.67% R (3/6, 1 UN)-50%	H(-), C(-), A(-), R(-)	H, C, A, R	H(+), C(+), A(+), R(-)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)
Aripiprazole	3/6 (++++), 2/6 (++) 1/6 (+)	H (3/6)-50% C (5/6)-83.33% A (3/6)-50% R (6/6)-100%	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)
Ziprasidone	5/6 (++++), 1/6 (+++)	HCA (6/6)-100% R (5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(-)	H(+), C(+), A(+), R(+)
Quetiapine	5/6 (++++), 1/6 (+++)	HAR (6/6)-100% C(5/6)-83.33%	H(+), C(+), A(+), R(+)	H(+), C(-), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)

Table 1. Continued 3

Psychotropic medication	Congruity between different databases	Congruity in positive interaction (%)	Medscape	WebMD	Drugs.com	Drugbank	Lexicomp	Liverpool COVID-19 interactions
Methylphenidate	1/6 (++), 4/6 (----), 1/6-UN	HAR (0/6, 1 UN)-0% C (1/6, 1 UN)-16.67%	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(+), A(-), R(-)	H(-), C(-), A(-), R(-)	H, C, A, R
Atomoxetine	1/6 (++++), 3/6 (++), 1/6 (----), 1/6-UN	H (1/6, 1 UN)-16.67% C (4/6, 1 UN)-66.67% A (2/6)-33.33% R (3/6)-50%	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(-), C(+), A(+), R(-)	H, C, A, R
Modafinil	1/6 (++++), 1/6 (++), 3/6 (+), 1/6-UN	H (0/6, 1 UN)-0% C (1/6, 1 UN)-16.67% A (2/6, 1 UN)-33.33% R (5/6, 1 UN)-83.33%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(+), R(+)	H(-), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H, C, A, R
Lorazepam	1/6 (++++), 1/6 (+), 4/6 (----)	H (1/6)-16.67% C (1/6)-16.67% A (1/6)-16.67% R (2/6)-33.33%	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)
Clonazepam	1/6 (++++), 1/6 (++++), 3/6 (+), 1/6 (----)	H (1/6)-16.67% C (2/6)-33.33% A (1/6)-16.67% R (5/6)-83.33%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(-), R(+)	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(+)
Diazepam	1/6 (++++), 1/6 (++), 4/6 (+)	H (1/6)-16.67% C (1/6)-16.67% A (2/6)-33.33% R (6/6)-100%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)
Alprazolam	1/6 (++) 5/6 (+)	H (0/6)-0% C (1/6)-16.67% A (0/6)-0% R (6/6)-100%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)
Buspirone	1/6 (++++), 4/6 (+), 1/6 (----)	H (1/6)-16.67% C (1/6)-16.67% A (0/6)-0% R (5/6)-83.33%	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(-)	H(+), C(+), A(-), R(+)	H(-), C(-), A(-), R(+)	H(-), C(-), A(-), R(+)
Propranolol	1/6 (++++), 4/6 (++), 1/6 (----)	H (2/6)-33.33% C (5/6)-83.33% A (1/6)-16.67% R (4/6)-66.67%	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(+), A(-), R(+)	H(-), C(-), A(-), R(-)	H(+), C(+), A(-), R(-)	H(+), C(+), A(+), R(+)
Naltrexone	2/6 (++) 3/6 (----) 1/6-UN	H (0/6)-0% C (1/6)-16.67% A (1/6)-16.67% R (2/6)-33.33%	H(-), C(-), A(-), R(-)	H(-), C(-), A(-), R(-)	H(-), C(-), A(+), R(+)	H(-), C(+), A(-), R(+)	H(-), C(-), A(-), R(-)	H, C, A, R
Promethazine	2/6 (++++), 2/6 (++++), 1/6 (----), 1/6-UN	H (2/6)-33.33% C (4/6)-66.67% A (4/6)-66.67% R (4/6)-66.67%	H(-), C(+), A(+), R(+)	H(-), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(+), C(+), A(+), R(+)	H(-), C(-), A(-), R(-)	H, C, A, R

H, hydroxychloroquine; C, chloroquine; A, azithromycin; R, ritonavir; +, symbol corresponds to presence of interaction; -, symbol corresponds to no potential interaction; UN, unknown.

mal interaction grade across databases except ritonavir which mostly shows moderate and severe interaction with other psychotropic medications. Hydroxychloroquine and azithromycin have least reported severe interactions across all six databases with 100% congruity for drug interaction

for eight psychotropic medications. Overall, safety profile of hydroxychloroquine is best as it has moderate and severe interactions (> 50% congruity) with eighteen psychotropic medications while ritonavir has worst profile with thirty-nine medications.

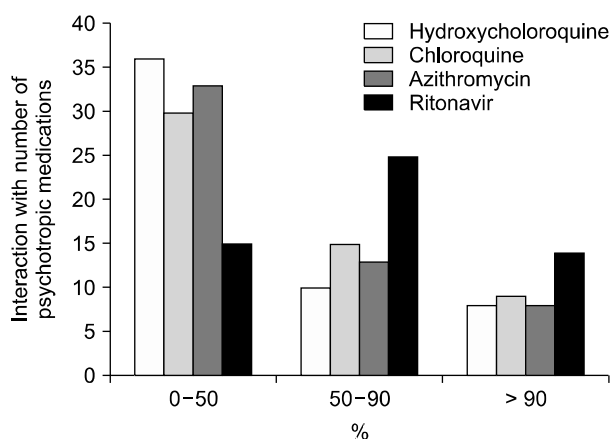


Fig. 2. Levels of drug interaction between COVID-19 drugs and psychotropic medications.

References and Grade of Evidence for the Studies Used for Reporting

The databases used for the recommendation were evaluated to ascertain the level of evidence used. Most popular databases like WebMD [6] and Medscape [7] just provided the result without referencing the source for the same.

I. The database Liverpool[®] Drug Interaction Group [11] for COVID-19 therapies (<https://covid19-druginteractions.org>), developed by the University of Liverpool provides the most extensive and detailed report after classifying every drug interaction into four categories and further categorizing the level of evidence using GRADE recommendations alongside a table reporting all the studies evaluated for the final consensus.

II. Lexicomp [8] is the second most comprehensive and complete database developed by Wolters Kluwer. The risk rating is done as A- no known interaction, B- no action needed, C- Monitor therapy, D- Consider therapy modification, X- Avoid combination. The product monograph provides discussion of available literature and includes PubMed indexed literature links but does not grade the evidence for some of the drug interactions.

III. Drugbank [9] also grades the severity as minor, moderate and major. Some of the references used are from standard Food and Drug Administration (FDA) guidelines while others have references from PubMed indexed studies or manufacturer's monograph. However, the level of evidence is not graded.

IV. Drugs.com [10] has two separate pages for every drug interaction- one for consumers and one for profes-

Table 2. SCOPE score evaluation for completeness of database

Databases	Interacting and non-interacting drug pairs (A)	Unavailable drug pairs (B)	SCOPE score (A/A + B)
Medscape	200	16	0.92
WebMD	200	16	0.92
Drugs.com	192	24	0.88
Drugbank	216	0	100
Lexicomp	212	4	0.98
Liverpool COVID-19 interactions	176	40	0.81
Total- 54*4=216 drug interactions			

sionals. The two varies in the type of explanation wherein the consumer tab provides information about potential risks and warning signs whereas professional tab details on the available references, classifies it as major/moderate/minor and also details on the management strategy. The references standards include European medicines agency, FDA and product manufacturer's monograph but the evidence is not graded.

Comparative Evaluation for Completeness of Database

SCOPE score evaluation revealed that Drugbank had all the assessed drug interactions (1.00) whereas Liverpool[®] Drug Interaction Group scored the least (0.81) (Table 2). Interaction of 54 commonly used psychotropic medications was evaluated with four medications used for management of COVID-19 (a total of $54 \times 4 = 216$ interactions). SCOPE score is calculated by dividing the total number of interactions available for a particular database by the total possible interactions (i.e., 216).

Comparative Evaluation of Databases

The overall evaluation of the databases was done based on their 'ease of understanding for consumers', 'ease of understanding for professionals', 'level of completeness', 'discussion on level of evidence', 'the number of available drugs', and 'congruity with other databases'. These items were graded on Likert scale from 1 (very poor) to 5 (excellent) by the authors of the study independently and their mean scores were calculated and tabulated thereafter. The evaluation of the databases on the specific parameters was done by a medical graduate (first author) and confirmed in discussion with psychiatry post-graduate residents (authors of this article) and a faculty of psychiatry. Overall, Liverpool[®] Drug Interaction Group

Table 3. Comparative evaluation of all the databases for psychotropic medication interaction with COVID-19 drugs

Parameters of evaluation	Medscape	WebMD	Drugs.com	Drugbank	Lexicomp	Liverpool COVID-19 interactions
Ease of understanding for consumers	2	2	5	3	4	4
Ease of understanding for professionals	2	2	5	3	4	5
Level of completeness	1	2	3	3	5	5
Level of evidence used and classified	1	1	3	3	4	5
Number of available drugs	2	3	3	5	4	1
Congruity with other databases	5	4	3	1	2	3
Average overall score	13/30	14/30	22/30	18/30	23/30	23/30

Likert scale (1- Very poor, 2- Poor, 3- Acceptable, 4- Good, 5- Excellent).

and Lexicomp scored the highest and were the best interaction checker software closely followed by Drugs.com. Drug bank also has a wide database. Medscape has the poorest interaction checker database without much collaborative evidence followed by WebMD (Table 3).

DISCUSSION

The findings of our study give a gross heterogeneity in the drug-drug interactions between the various online data bases compared, which indicate that information related to drug-drug interaction in the data bases must be referring to different resources or evidences. High congruency in drug-drug interaction is found for some psychotropic medications like – escitalopram, citalopram, clomipramine, amitriptyline, Clozapine, Olanzapine, Ziprasidone, Quetiapine, Lamotrigine, Haloperidol, Trihexyphenidyl, Acamprosate and Alprazolam. It might be due to extensive research exiting on these drugs, and consistent pattern of drug-drug interactions reported across the researches.

Our findings included significant incongruity between different databases similar to previous studies [12,13]. Ritonavir being a pan CYP inducer had the maximum moderate to severe drug interactions reported, similar to another study on comparison of antipsychotic drugs with COVID-19 medications [12]. The most reliable databases for checking psychotropic drug interactions with COVID-19 drugs (used in the 1st wave) was Liverpool[®] Drug Interaction Group and Lexicomp. Overall, Lexicomp had a wider and more comprehensive database at present with a high SCOPE score, which can be easily used by healthcare professionals. Our findings are further strength-

ened by other similar studies addressing drug-drug interactions. However, it had discrepancy with other databases due to infrequent updates of the available studies on the subject, along with a subscription cost associated with it.

The Liverpool[®] Drug Interaction Group has also developed separate software for addressing other important drug interactions. It uses GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) recommendations for classifying the available studies on the interactions, classifies most of the clinically important ones and provides freely accessible pdf for each drug interaction checked. However, it also faces the drawback of frequently missing or unavailable data. If it is updated rigorously, it can prove to be the most comprehensive drug interaction database for free use by both healthcare professionals and pharmacists.

For patients, Drugs.com can serve as an efficient alternative which not only details on the drug interactions in a simple language but also warns against red flag symptoms.

This study has several implications for healthcare professionals, care givers, patients, and pharmacists. For healthcare professionals including consultants, residents, and nurses, it is imperative to grade and classify the information available freely through these databases. In most of the low and low- and middle-income countries, the provision of a standardized institutional access database like Stockley's drug interactions in the UK and the USA is limited. The high individual out-of-pocket subscription costs are prohibitory to its widespread use especially by residents and interns. Finding the needful in-

teractions in standard textbooks available for reference like is difficult due to the adoption of organ-system based classification and infrequent updates.

For ease of availability and accessibility along with the lack of knowledge regarding standard references, care givers and patients use these online freely available databases. However, the most widely used resources like Medscape and WebMD do not refer sources which undermines their authenticity as evident by our study as well.

For trained pharmacists, it is also imperative to keep themselves abreast of the recent studies in the field and rely on their practicing knowledge. Pharmacists are not available in several resource limited settings and incorrect prescription of drugs due to constraints of time and knowledge leads to life-threatening reactions which could be prevented by using the most updated database.

The limitations of our study include assessment of the drug-drug interactions (DDI) cross-sectionally across the available databases and exclusion of paid databases for which we did not have institutional access. Apart from Liverpool[®] Drug Interaction Group, we did not classify the available references based on GRADE recommendations. The use of online database can prove beneficial but the lack of agreement/congruity between the different databases effects its reliability. While using online databases, healthcare workers should use the most comprehensive and reliable database available.

In conclusion, there was significant variability in the recommendations available on different databases regarding concomitant prescribing of psychotropic medications with drugs used during first COVID wave. Ritonavir reported the maximum drug interactions with most of them graded as severe. The freely accessible software Liverpool[®] Drug Interaction Group developed by University of Liverpool was one of the most reliable databases but had the drawback of frequently missing data on several drugs. Lexicomp had the most comprehensible database but had significant variability than other databases due to limited updates. Drugs.com was fairly reliable and easy to understand tool for patients. WebMD and Medscape were the least reliable sources.

■ Funding

None.

■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Sujita Kumar Kar. Data acquisition: Surobhi Chatterjee, Sujita Kumar Kar, Aathira Jaya Prakash, Teena Bansal, Garima Singh. Formal analysis: Surobhi Chatterjee, Sujita Kumar Kar. Supervision: Sujita Kumar Kar. Writing—original draft: Surobhi Chatterjee, Sujita Kumar Kar. Writing—review & editing: Surobhi Chatterjee, Sujita Kumar Kar, Aathira Jaya Prakash, Teena Bansal, Garima Singh.

■ ORCID

Surobhi Chatterjee <https://orcid.org/0000-0003-1975-5107>
 Sujita Kumar Kar <https://orcid.org/0000-0003-1107-3021>
 Aathira Jaya Prakash <https://orcid.org/0000-0002-3794-8589>
 Teena Bansal <https://orcid.org/0000-0002-7277-4262>
 Garima Singh <https://orcid.org/0009-0009-8158-096X>

REFERENCES

1. van Roon EN, Flikweert S, le Comte M, Langendijk PN, Kwee-Zuiderwijk WJ, Smits P, et al. *Clinical relevance of drug-drug interactions: A structured assessment procedure. Drug Saf* 2005;28:1131-1139.
2. Zhang L, Zhang YD, Zhao P, Huang SM. *Predicting drug-drug interactions: An FDA perspective. AAPS J* 2009;11:300-306.
3. Monteith S, Glenn T. *A comparison of potential psychiatric drug interactions from six drug interaction database programs. Psychiatry Res* 2019;275:366-372.
4. Kar KS, Yasir Arafat SM, Kabir R, Sharma P, Saxena SK. *Coping with mental health challenges during COVID-19. In: Saxena SK, editor. Coronavirus disease 2019 (COVID-19): Epidemiology, pathogenesis, diagnosis, and therapeutics. Singapore: Springer;2020. p.199-213.*
5. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. *Pharmacologic treatments for coronavirus disease 2019 (COVID-19): A review. JAMA* 2020;323:1824-1836.
6. *Drugs interaction checker- find interactions between medications [Internet]. WebMD LLC.; 2020 [cited at 2022 Mar 26]. Available from: <https://www.webmd.com/interaction-checker/default.htm>.*
7. *Drugs interaction checker- medscape drug reference database [Internet]. WebMD LLC.; 2020 [cited at 2022 Mar 26]. Available from: <https://reference.medscape.com/drug-interactionchecker>.*
8. *Lexicomp: Evidence-based drug referential content [Internet]. Wolters Kluwer; 2020 [cited at 2022 Mar 26]. Available from: <https://www.wolterskluwer.com/en/solutions/lexicomp>.*

9. Wishart DS, Feunang YD, Guo AC, Lo EJ, Marcu A, Grant JR, et al. *DrugBank 5.0: A major update to the DrugBank database for 2018*. *Nucleic Acids Res* 2018;46:D1074-D1082.
10. *Prescription drug information, interactions & side effects [Internet]*. *Drugs.com*; 2020 [cited at 2022 Mar 26]. Available from: <https://www.drugs.com/>.
11. *Liverpool COVID-19 interactions [Internet]*. *Liverpool: University of Liverpool*; 2020 [cited at 2022 Mar 26]. Available from: <https://www.covid19-druginteractions.org/>.
12. Plasencia-García BO, Rodríguez-Menéndez G, Rico-Rangel MI, Rubio-García A, Torelló-Iserte J, Crespo-Facorro B. *Drug-drug interactions between COVID-19 treatments and anti-psychotics drugs: Integrated evidence from 4 databases and a systematic review*. *Psychopharmacology (Berl)* 2021;238:329-340.
13. Vitry AI. *Comparative assessment of four drug interaction compendia*. *Br J Clin Pharmacol* 2007;63:709-714.