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Review Article

Adverse Drug Reaction Tools Used in Causality Assessment

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ABSTRACT

Adverse Drug Reactions (ADRs) tools are very significant in the detection, assessment, and severity of ADRs. This review emphasizes the most frequently utilized causality assessment scales, for example, the WHO-Uppsala Monitoring Centre Causality Assessment System, the Naranjo algorithm for the ADR assessment, the Liverpool Causality Assessment Tool (LCAT), and the Roussel Uclaf Causality Assessment Method (RUCAM). Bayesian Adverse Reactions Diagnostic Instrument (BARDI). In this review we found that the most commonly preferred tool is Naranjo Algorithm and the most commonly used combination is the WHO-Uppsala Monitoring Centre causality assessment system and the Naranjo algorithm. Large numbers of causality appraisal strategies have their benefits and burdens. In any case, Due to variation and inconsistency, no single causality assessment measure has been accepted and utilised globally. No single scale, however, has been accepted as standardised and taken into consideration for widespread acceptability.

Keywords: Adverse Drug Reaction, Causality assessment tools, Naranjo algorithm, WHO-Uppsala Monitoring Centre causality assessment system.

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INTRODUCTION

WHO defines an Adverse Drug Reaction (ADR) as "a toxic, unanticipated drug reaction that occurs at doses typically used in humans for disease prevention, diagnosis, therapy, or alteration of physiological function". One of the primary causes of mortality and morbidity in hospitalized patients is unfavorable medication responses.[1] Pharmacovigilance (PV) is a fundamental part of the science which is associated with the collection, detection, assessment, understanding, and avoidance of unfavorable impacts or a few other issues with drug use.[2] The idea of drug safety/pharmacovigilance is raising different drug effects to people's attention. The development of Adverse Drug Reactions assessment tools to gather ADR reports and assess the safety of promoted drugs is vital to assist medical care experts with studying drugs and guaranteeing their well-being.[3] The occurrence of ADR revealed by different studies across the world is 6-20%, while in India, it depends at 3%. Hospitalised patients account for about 10–20% of ADRs, which lengthens hospital stays.[4]

Clinicians, academics, the pharmaceutical industry, and regulators all analyse the causality of ADRs in various contexts, including clinical trials. It's critical to establish a causal link between a medicine and a pharmaceutical response in order to stop future occurrences. Causality Assessment (CA) evaluates the likelihood that a particular therapy is to blame for a noted adverse event.[5] The CA of Adverse Occurrences (AEs) can be done using a variety of methods, such as expert judgement, Bayesian procedures, algorithms, and scales. In any event, there isn't a single tool that is universally accepted or regarded as the gold standard.[6] The Swedish method, the WHO Uppsala Monitoring Centre (UMC) scale, Naranjo's Algorithm (NA), the Kramer and Jones calculations, the Karch algorithm, and the Bégaud algorithm are all included in these. algorithm Warning Board rules, Bayesian Adverse Reaction Diagnostic Instrument, thus on.[7,8] Naranjo's calculation and WHO UMC scales are generally accepted and the most widely used methods and techniques for causality evaluation in clinical practice as they offer a simple methodology.[5,9]

Finding the cause of an occurrence and its connection to drug usage is crucial in 1981, the Naranjo ADR Probability Scale was created.[10] An ADR's likelihood depends on its attributes, rate, the accuracy of the data, and the scale employed. Initially used to evaluate ADR, the WHO-UMC scale has subsequently been replaced by the Naranjo ADR Probability Scale. whose broad variety of questions gives the impression that it is more authentic and predictable. A review of medical records is necessary, and a clinical history should be obtained whenever practical. It is recommended to perform allergen skin testing to look for anaphylactic symptoms and quick reactions.[11]

Casual causality evaluation of ADRs is in regular practice by clinical benefits specialists to close choice decisions as to the

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treatment of the executives. Calculations ought to give a more genuine decision on causality rather than a theoretical explanation in perceiving unfavorable occasions during treatment. The four fundamental principles essential to the objective causal assessment consolidate 1) transient qualification, 2) DE challenge and result, 3) rechallenge and result, and 4) confounding factors.[2]

The lack of information regarding the safety and effectiveness of recently produced drugs and vaccines highlights the necessity of post-marketing surveillance.[12] Pharmacovigilance plays a main role that is crucial in ensuring patient safety and the proper administration of medications, which is the process of ongoing safety monitoring. The primary approach for discovering previously unrecognized, unusual, or unexpected ADRs and for routinely evaluating the risk-benefit ratio of some medications is the spontaneous reporting system.[13] With spontaneous reporting systems, Clinical Pharmacists, manufacturers, and patients voluntarily report suspected ADRs. The effectiveness of post-marketing surveillance depends on Health care professionals and patients reporting ADRs.[12]

Predictable and unpredictable are the two main categories of ADRs. Depending on the harm they do to the patient, adverse medication reactions can range from moderate to severe.[14] Adverse drug reactions are the fifth-leading cause of death globally; they are also liable for hospitalizations. ADR has clear risk factors that can be divided into four categories: patient-related, drug-related, disease-related, and social-related.[15] The majority of ADRs result from prescription errors, drug interactions, polypharmacy, patient compliance, and occasionally from the use of fake or substandard medications. Undesirable responses that happen because of conscious extreme or unplanned dose and maladministration can be considered an adverse event.[16]

ADR monitoring is essential in the hospital context because it aids in understanding the nature and types of ADRs and identifies patients who are at a greater risk of getting ADRs. ADR monitoring is used less frequently in emerging nations. For instance, while industrialized nations have an average ADR monitoring rate of 5%, India only has a 1% rate.[15] To achieve the pharmacovigilance goals, healthcare professionals must be engaged. Healthcare professionals may not report ADRs because of guilt, a lack of awareness, motivation, ignorance, a lack of training, or time.[17]

Causality assessment tools are significant for assessing the connection between a medication and an unfavorable occasion. These scales and algorithms can assist healthcare professionals in coming to informed conclusions about drug safety and can also aid in regulatory decision-making. There are a few causality assessment tools available, going from basic algorithms to additional complicated frameworks consolidating various standards. The decision of the tool depends upon the particular circumstance and the accessible information. In any case, it is critical to remember that causality assessment isn't always straightforward, and different variables can add to unfavorable occasions. Hence, the consequences of a causality assessment should be interpreted with regard to the individual patient and the available proof.

MATERIALS AND METHODS

Using keywords, such as "causality assessment scales," "causality evaluation", "methods for causality assessment", "tools for causality assessment", and "algorithm for causality" this relevant review finds out by the search engines Google, and Google Scholar, PubMed, Science Direct, and other literature published from 2019 to March 2023. These studies were conducted by Clinical Pharmacists with the help of other healthcare providers to assess the ADRs in hospitalized patients.

Author name	Methodology	Number of patients	Causality assessment	Result
Behailu Terefe Tesfaye[18]	A prospective observational study.	240 patients	Modified Naranjo Causality Scale (MONARCHS). The seriousness of the ADRs was sorted in view based on the modified Hartwig Severity Assessment Scale.	In complete, 64 ADRs were recorded. According to the Naranjo scale for looking over ADR causation, 15.5% of ADRs were definite, 68.9% were probable, and 15.5% were possible. As indicated by the altered Hartwig ADR severity assessment scale, 43.7% of ADRs were mild, 54.7% ADEs were moderate, and 1.6% ADEs were severe.

Author name	Methodology	Number of patients	Causality assessment	Result
Syed Arman Rabbani[19]	A prospective observational study.	150 grown-up CKD patients.	ADRs were evaluated utilizing Naranjo and WHO likelihood scales.	35 ADRs evidently were found in 25 CKD patients. Majority of obtained ADRs were possible (60 % by the Naranjo scale; 48.5 % of ADRs according to the WHO scale) followed by moderate severity (57 %), predictable (66 %), and not preventable (66 %) type. For the management of ADRs, the associated drug was removed in the greater part of the cases (77.1 %). Specific treatment was given to close to half of the patients (48 %) who experienced ADRs during the study period.
Fuad Adem[20]	An emergency hospital-based prospective observational study.	141 participants.	Naranjo ADR Probability Scale.	Naranjo ADR Probability Scale Six of the 14 ADRs found were using the Naranjo ADR assessment measure, scoring a 4 on the scale (possible ADR). Enalapril (five cases), metformin (four cases), hydrochlorothiazide (three cases), digoxin (one case), and nifedipine were the medications connected to ADR during the perioperative admission (one case).
Parminder Nain[16]	A prospective and observational study.	250 patients.	ADR is recognized by the Naranjo size of causality. Severity categorized by the Modified Hartwig Scale.	Completely out of 52 ADRs were seen, with the overall prescription probable (61.53%), possible (34.61%), definite (1.92%), and unlikely (1.92%). 34.61% of the reactions fell into the Level 3 classification. Of all reactions, 17 (32.69%) were Level 4A responses. There was an amount of eight (15.38%), six (11.55%), one (1.92%), and one (1.92%) reaction from various levels, which compared to the Level 2, Level 4B, and Level 5 grades, separately.
Samuel Berihun Dagnew[21]	A multicentre prospective observational study.	389 patients	Naranjo Algorithm of adverse drug reaction probability scale.	There were 96 ADRs on the whole (82 were actual and 14 were possible ADRs). Based on the Naranjo assessment scale, 41 (half) patients had probable and 33 (40%) followed by 7 (9%), and 1 (1%) had possible, definite, and doubtful ADR.
K. C. Bharath Raj[15]	It is a prospective observational study conducted over six months.	385 patients	Causality assessment using the WHO probability scale and Naranjo's Scale. The severity level is assessed using Hartwig's Severity Assessment Scale.	Record of 34 ADRs found in 385 patients, The Naranjo's causality scale shows that a large portion of the ADRs was probable 22 (64.7%), considering that 8 (23.5%) reactions were possible and 4 (11.80%) reactions were definite. According to the WHO's causality evaluation, most of the reactions—15 (44.1%)—were probable, while 10 (29.4%) were certain, 8 (23.5%) were possible, and 1 (2.9%) were restrictive. Hartwig severity scale was used to review the severity of the thought ADRs, and it was seen that 15 (44.1%) reactions were mild, while 19 (55.9%) reactions were moderate.

Author name	Methodology	Number of patients	Causality assessment	Result
Parihar Ashish Singh[22]	It was a prospective, observational study.	286 selected patients.	Causality assessment is done by a Naranjo Probability Assessment Scale. The severity of ADR has been assessed by Hartwig's Severity Assessment Scale.	27 patients were related to ADR the most notable ADRs were hand tremors and hypothyroidism. On causality assessment, 44.4% of cases were probable and possible. Generally speaking, the reality of ADR was laid out at Level III at 74.7% and Level II at 25.9%. The rate of affirmation of pharmacist intervention by a therapist is 74.7%. The critical justification for ADR was drug/dose assurance (74.07%).
Mounika Nirumalla[23]	A prospective unconstrained study.	A study was done on 65 patients in all branches for a period of 6 months	Naranjo Algorithm of ADR probability scale. The severity of ADR has been assessed by Hartwig's Severity Assessment Scale	38 of the patients who experienced ADRs. Causality evaluation of ADR' given Naranjo scale Seriousness probable 45 (69.23) possible 20(30.76) trailed by Doubtful, Definite. Considering the WHO-UMC Scale Earnestness Certain 03 (4.6) probable 19 (29.23) possible 43 (66.15). In the modified Hartwig and Siegel scale severity is mild 14 (21.5) Moderate 48 (73.8) Extreme 03 (4.61).
Siraj Sundaran[24]	This prospective companion studies.	51 ADRs were detected among 49 patients.	Causality assessment done by Naranjo's Algorithm scale, severity using the Modified Hartwig and Siegel scale.	51 ADRs were recognized among 49 patients. According to the causality assessment, most of the ADRs were probable (n = 26, 51.0%), and type A (expanded/pharmacological) reactions (n = 39, 76%) were the most broadly recognized kind of ADR found. The majority of ADRs (n = 35, 68.6%) were moderate to serious; of these, 37.3% were deemed possibly preventable. A further treatment/ cure was given to oversee ADRs, and 29.4% of the medications that were considered were stopped, followed by another 29.4% of prescriptions.
Sathvik Belagodu Sridhar[25]	A prospective study conducted in the nephrology unit	378 patients	World Health Organization (WHO) probability scale, Naranjo's algorithm, Karch then Lasagna's scale.	The causality of thought ADRs was viewed as probable, possible, and unassessable for 27 (60%), 17 (37.7%), and one ADRs (2.2%), separately, when assessed by the World Health Organization (WHO) probability scale. As indicated by Naranjo's calculation, 26 ADRs (57.7%) were delegated as possible followed by 19 ADRs as probable (42.2%). In actuality, when Karch and Lasagna's scale was applied to determine the causality of the ADRs, the idea of ADRs for most of the ADRs was possible (n = 33, 73.3%) followed by probable (n = 12, 26.6%) Around 26 ADRs (57.7%) and 19 ADRs (42.2%) were viewed as predictable and unpredictable in nature, separately. Around 30 ADRs (66.6%) were certainly preventable and 13 ADRs (28.8%) were most likely preventable. Of 45 ADRs, 18 (40%) and 19 (42.2%) ADRs were viewed as mild and moderate in severity, separately.

Author name	Methodology	Number of patients	Causality assessment	Result
Pulimi Divya Priyanka[26]	The Prospective, observational study.	600 patients	Naranjo's Scale algorithm.	A complete number of 374 ADRs were accounted for in 600 patients. As indicated by Naranjo's calculation Probable are:193, followed by possible:84, definite:80, doubtful:16 The larger part of the ADRs [95 (74.80%)] was managed by withdrawing the suspected drug.
JERIN JAMES[27]	A prospective spontaneous reporting study.	230 patients	Naranjo scale.	Throughout the course of the investigation, 80 ADRs in total were recorded. 15% of the responses were reported using Naranjo Scale, while 85% of the responses were probable. According to the modified Hartwig's criteria, the vast majority of the reactions (75%) were mild.
Tadele Mekuriya Yadesa[28]	A prospective cohort study.	124 participants	Naranjo ADR causality scale.	90 ADRs during the current hospital stay. ADRs were classified as probable 68 (75.6%), possible 19 (21.1%), and definite 3 (3.3%) ADRs using the Naranjo ADR causality scale.

We utilized a sum of 13 articles, in the review led by a clinical pharmacist it was found that the most regularly utilized ADR evaluation scale is the Naranjo Calculation[10] followed by a blend of scale WHO-UMC and Naranjo calculation[3] so here we know that the greater part of them favoured Naranjo calculation since it is simple and helpful to utilize yet as of recently, not a solitary causality evaluation scale has been acknowledged and adopted universally due to variability and inconsistency. No single scale, in any case, has been acknowledged as standardized and taken into consideration for widespread acceptance. The Naranjo likelihood scale and the WHO causality assessment scale are frequently utilized and suggested in many settings. Among the saw ADRs the thought drugs were halted, then, at that point, another prescription was eliminated, and an additional treatment/fix was given to oversee ADRs. causality evaluation in such cases adds to i) early recognition of ADRs and minimization of extra disarray ii) optimized treatment; iii) new strategical management to keep away from repeat iv) Cost minimization by reducing delayed hospitalization.

Pharmacovigilance is handled by the Clinical Pharmacy practice department in the majority of hospitals in India. The clinical pharmacist or pharmacologist, clinician other medical services experts is consistently available to answer questions connected with ADR in significant hospitals.[11] The following flow chart explains how healthcare providers work or contribute to the field of ADR. In each and every process they will assess and anticipate patient safety, and check the severity of adverse effects by using suitable causality assessment tools.

Causality assessment

Causality evaluation of Adverse Drug Reactions (ADRs) includes deciding the probability of a causal connection between a medication and an unfavorable drug effect. In an early study, it was seen that there are 34 exceptional procedures for the causality assessment of ADRs.[29] ADRs are accidental and unsafe impacts that happen when a patient is taking medication, these scales and algorithms are used to assess the ADRs, and drug safety:

- The Wilholm *et al*. Method 1984.
- Dangaumou's french method.
- Kramer *et al*. 1974 method.
- Lagier *et al*. method / Balanced assessment method (Lagier *et al*. 1983).
- STP: Summary time plot/Castle *et al* method (Castle *et al*. 1984).
- Cibageigy method (Venulet *et al*.1980).
- Loupi *et al*. 1986 method.
- M and V Scale: The Maria and Victorino scale.
- Australian method.
- The WHO-UMC: WHO-Uppsala Monitoring Centre causality assessment system.
- Drug Interaction Probability Scale (DIPS).
- Bayesian Adverse Reactions Diagnostic Instrument (BARDI).
- MacBARDI spreadsheet.

- Causality assessment of vaccine-related adverse events.
- Karch and lasagna scale.
- Begaud algorithm.
- Hallas scale.
- PRISCUS list.
- RUCAM scale.
- CIOMS scale.
- Liverpool ADR scale.
- VAS: Visual Analogue Scale (Miremont *et al.* 1994).
- Blanc *et al.*
- Emanueli and sacchetti.
- Stephen's algorithm.

Most commonly using ADR tools

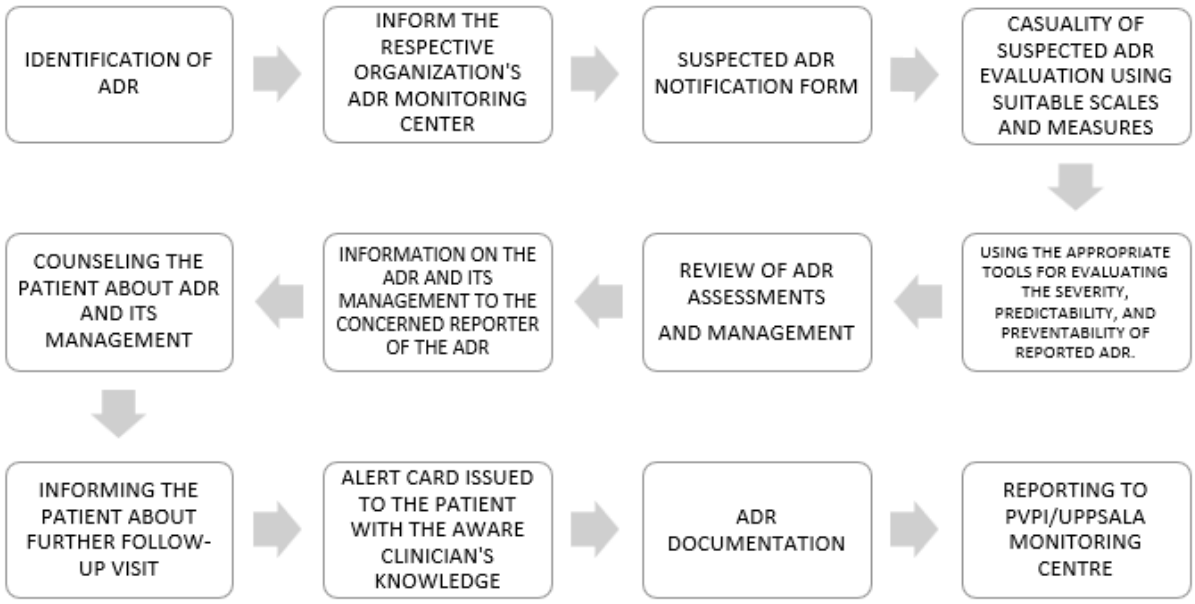
There are a few commonly used scales that have been created for causality assessment, including the Naranjo algorithm, the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) system, the Liverpool Causality Assessment Tool (LCAT), and the Roussel Uclaf Causality Assessment Method (RUCAM). Bayesian Adverse Reactions Diagnostic Instrument (BARDI).

1. Naranjo algorithm: The Naranjo algorithm, also called the Naranjo Scale, was created in 1991 by Naranjo *et al.* at the College of Toronto. This scale was developed to help standardise the assessment of cause for all ADRs. Additionally, rather than being used in standard clinical practise, the scale was designed for use in controlled trials and registration studies of novel medications. In any case, it is widely used and simple to apply.[9] Naranjo Scale (NS), one of the CA scales, is frequently used since it is simple to use. ADR monitoring technology was initially developed to be used in clinical trials and registration trials of new drugs.[6] This 10-item questionnaire gives scores to many aspects, including the timing of drug exposure and the commencement of the ADR, the existence of external causes, and prior reports of the same reaction to the same drug. The final score represents the likelihood of a causal connection between the drug and the ADR after the scores have been added together.[30] The reply to each address gets a score. The all-out score goes from 4 to 13. A score of at least 9 shows a clear ADR, a score of 5 to 8 probable ADR, a score of 1 to 4 shows a possible ADR, and a doubt of 0 or less. After that assess whether the patient outcome recovered or not recovered.[31,32]

Limitation: The Naranjo Scale misses out on key information needed to evaluate the causality of potential medication interactions.[22,23]

2. WHO-UMC system: The WHO causality evaluation scale is a significantly involved scale for the evaluation of the causal relationship of case reports and has been created during the Global Medication Checking Program in conversation with national centers. The WHO-UMC method divides ADRs into four groups depending on the timing, nature, and recurrence of the reaction as well as the drug's recognized pharmacological characteristics. Certain, Probable/Likely, Possible, and Unlikely are the classifications.[23,33]

This scale has been classified into 6 groups considering the essential rules of 4 necessities in every classification. These 4



ADR monitoring and management procedure

standards integrate a) transient relationship b) validity and nonappearance of different variables c) lab revelations and d) de-challenge and once again challenge. Unclassified is pertinent when additional information is vital to evaluate the relationship.[2]

Limitations: high reliance on individual expertise and judgment for evaluation, delicate and unfortunate reproducibility in the WHOUMC system, and also individual classes are not strongly described.[7]

3. LCAT: The Liverpool ADR causality assessment instrument was made by Gallagher *et al*. in view of the norms spread out by Sir Branford Slope. They exhibited similar results with a couple of variable debates with the Naranjo scale and high inter-rater reliability (IRR). This scale has a stream chart game plan instead of a scoring framework, which makes assessing more straightforward and faster.[34] This 9-item questionnaire evaluates the presence of alternate causes, the outcomes of diagnostic testing, and the temporal link between drug exposure and the onset of the ADR. The final score represents the probability that the drug and the ADR are causally related.[35,36]

Limitation: The tool's validation was conducted internally rather than independently. This scale requires additional validation and expert assurance of outcomes.[37]

4. Bayesian Adverse Reactions Diagnostic Instrument (BARDI): The BARDI approach was created to overcome the constraints of variability using expert judgment and algorithms. This procedure surveys back opportunities for thoroughly considered drugs and other substitute elements. The back odd component comprises around six subsets of examination; the primary subset (prior possibilities) oversees epidemiological data, and clinical preliminary information and This technique assesses back chances for thought drugs over other alternate factors. The posterior odd element consists of about six subsets of appraisal; the first subset (earlier chances) manages epidemiological information, clinical trial data, and population pharmacokinetics, while the other five subsets (likelihood proportions) manage explicit case report data.[38]

Limitation: While being run by professionals, results can show multiple causal relationships between drugs and events.[2]

5. RUCAM: To assess the causative link between medications and liver injury, the Roussel Uclaf Causality Assessment Method (RUCAM) is frequently utilized. It can be used to evaluate hepatotoxic medications that are being developed in clinical trial settings in an objective manner. This 10-item survey evaluates parameters such as the timing of drug exposure and the commencement of the ADR, the existence of additional causes, and the outcomes of laboratory testing. The final score assigns a category of causation ranging from "definite" to "unlikely," as well as the likelihood of a causal connection between the drug and the ADR.[39,40]

Limitation: The scoring framework doesn't consolidate variables old enough, liquor reliance, and different elements that affect the consequences of the causal relationship of medications with hepatic injury. When dealing with the unpredictability of results and removing additional causes of liver injury, the scale may occasionally need to be fabricated.[2]

Severity Assessment Scale

1. Hartwig's Severity Evaluation Scale: A tool used to evaluate the severity of Adverse Drug Reactions (ADRs) in patients is Hartwig's Severity Evaluation Scale. Based on the clinical effects of the ADR rather than the cause or type of ADR, it has six levels of severity that range from moderate to lethal. It is frequently employed in clinical practice and research to compare the severity of various ADRs or to track the severity of ADRs over time.[41,42]

These scales and algorithms can be helpful in determining the causality and severity of ADRs, but they should be used in conjunction with clinical judgment and other available evidence. A comprehensive examination of the data is necessary because no scale or method can provide a conclusive solution to causality.[43]

CONCLUSION

The reason ADRs use a range of tools and procedures, including the WHO-UMC system and the Naranjo Algorithm, each of which has advantages and disadvantages. Because of variation and irregularity in the reliability and validity, as of late, not a single causality evaluation scale has been approved and adopted generally. The WHO-UMC scale is recommended by the PvPI, however many primary care physicians choose the straightforward Naranjo calculation. In examining ADRs, terrible reproducibility and varying degrees of arrangement have been observed among distinct CATs. A globally accepted objective causality assessment scale must be created since causality evaluation is a crucial component of the pharmacovigilance cycle. Future examinations can be arranged where interrater fluctuation can be surveyed utilizing similar scales. Further studies are anticipated to develop the gold standard method strategy for the causality assessment of ADRs.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Rallabandi SS, Makula SS, Sindgi VM, Babu BJ, Puneem US. [Monitoring adverse effects of antipsychotics and antidepressants: A population based study]. Indian J Pharm Pract. 2021;14(3):191-7. doi: 10.5530/ijopp.14.3.38.
2. Ap K, Bhoopathi D, Sunkara H, Chalasani Sh. An overview of various scales used in causality assessment of adverse drug reactions. Int J Pharm Pharm Sci. 2020:1-5.
3. Lan T, Wang H, Li X, Yin H, Shao D, Jiang Y, *et al.* The effect of clinical pharmacists' intervention in adverse drug reaction reporting: A retrospective analysis with A 9-year interrupted time series. BMC Health Serv Res. 2022;22(1):925. doi: 10.1186/s12913-022-08320-8, PMID 35854263.
4. Shukla AK, Jhaj R, Misra S, Ahmed SN, Nanda M, Chaudhary D. Agreement between who-Umc causality scale and the Naranjo algorithm for causality assessment of

adverse drug reactions. J Fam Med Prim Care. 2021;10(9):3303-8. doi: 10.4103/jfmpc.jfmpc_831_21, PMID 34760748.

5. Beniwal R, Gupta LK, Khare AK, Mittal A, Mehta S, Balai M. Clinical profile and comparison of causality assessment tools in cutaneous adverse drug reactions. Indian Dermatol Online J. 2019;10(1):27-33. doi: 10.4103/idoj.IDOJ_207_18, PMID 30775295.
6. Awase A, Joshi A, Patil V, Noronha V, *et al.* Validation of A Novel Causality Assessment Scale for Adverse Events in Non-Small Cell Lung Carcinoma Patients Treated with Platinum and Pemetrexed Doublet Chemotherapy. Sharma Jb, Krishnamurthy Mn. Ther Adv Drug Saf. 2021;12.
7. Behera SK, Das S, Xavier AS, Velupula S, Sandhiya S. Comparison of different methods for causality assessment of adverse drug reactions. Int J Clin Pharm. 2018;40(4):903-10. doi: 10.1007/s11096-018-0694-9, PMID 30051231.
8. Mascolo A, Scavone C, Sessa M, Di Mauro G, Cimmaruta D, Orlando V, *et al.* Can causality assessment fulfill the new European definition of adverse drug reaction? A review of methods used in spontaneous reporting. Pharmacol Res. 2017;123:122-9. doi: 10.1016/j.phrs.2017.07.005, PMID 28694146.
9. Naidu RP. Causality assessment: A brief insight into practices in pharmaceutical industry. Perspect Clin Res. 2013;4(4):233-6. doi: 10.4103/2229-3485.120173, PMID 24312892.
10. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45. doi: 10.1038/clpt.1981.154, PMID 7249508.
11. Verman S, Anjankar A. A narrative review of adverse event detection, monitoring, and prevention in Indian hospitals. Cureus. 2022;14(9):e29162. doi: 10.7759/cureus.29162, PMID 36258971.
12. Curtolo E, Szijj JV, Camilleri L, Serracino-Inglott A, Azzopardi LM. Development, validation and evaluation of learning activities to support the reporting of adverse drug reactions during the Covid-19 pandemic. Pharm Educ. 2022;22(1):515-22. doi: 10.46542/pe.2022.221.515522.
13. Li C, Xu T, Zhou P, Zhang J, Guan G, Zhang H, *et al.* Post-marketing safety surveillance and re-evaluation of Xueshuantong injection. BMC Complement Altern Med. 2018;18(1):277. doi: 10.1186/s12906-018-2329-z, PMID 30326892.
14. Yerni Kumar B, Guntapalli C, Rao K. Gsn, Kishore Kumar K, Rajsekar A. Medication reconciliation led by clinical pharmacist as an effective strategy in preventing and reducing adverse drug reactions. J Drug Alcohol Res. 2022;11(10).
15. Hassan S, Uu K, Mascarenhas V, Suresh G. Raj Kcb, Nayak P. A prospective study on adverse drug reactions in inpatients of general medicine department in A tertiary Care Hospital- A clinical pharmacist-led study. J Pharm Res Int. 2021:111-22.
16. Lalthanpuii K, Kaur J, Saini S, Bhatti K, Nain P. Strengthen the monitoring and reporting of adverse drug reaction at A tertiary teaching hospital. Arch Pharm Pract. 2022;13(1):61-7. doi: 10.51847/Zq3HaDzGqf.
17. Sankhi S, Marasine NR, Sankhi S, Lamichhane R. Adverse Drug Reaction due to Antidepressants among Patients with Depression in a Private Psychiatric Hospital of Nepal. BioMed Res Int. 2020; 2020:6682928. doi: 10.1155/2020/6682928, PMID 33294450.
18. Ta E, Yizengaw Ma TBt. Incidence of adverse drug events in patients hospitalized in the Medical Wards of a Teaching Referral Hospital in Ethiopia: A prospective observational study. BMC Pharmacol Toxicol. 2022;23(1).
19. Hammoud KM, Sridhar SB, Rabbani SA, Kurian MT. Evaluation of potential drug-drug interactions and adverse drug reactions among chronic kidney disease patients: an experience from United Arab Emirates. Trop J Pharm Res. 2022;21(4):853-61. doi: 10.4314/tjpr.v21i4.24.
20. Mohammed M, Bayissa B, Getachew M, Adem F. Drug-related problems and determinants among elective surgical patients: A prospective observational study. SAGE Open Med. 2022;10:205031212211224:20503121221122438. doi: 10.1177/20503121221122438, PMID 36093421.
21. Dagnew SB, Binega Mekonnen G, Gebeye Zeleke E, Agegnew Wondm S, Yimer Tadesse T. Clinical Pharmacist Intervention on Drug-Related Problems among Elderly Patients Admitted to Medical Wards of Northwest Ethiopia Comprehensive Specialized Hospitals: a Multicenter Prospective, Observational Study. BioMed Res Int. 2022; 2022:8742998. doi: 10.1155/2022/8742998, PMID 35898673.
22. Ashish Singh P, Ganachari Madiwalayya S, Tekkalaki Bheemsain V. Clinical Pharmacist Assessment in Monitoring and Resolving the Adverse Drug Reaction in Bipolar Disorder Patients: A Prospective, Observational Study at Tertiary Care Teaching Hospital; 2019. Available from: Http://Www.Ijournalhs.Org.
23. Nirumalla M, Veda Bobbili S, Krishnan Unni V, Sanapala S, Prathyusha P. A prospective study of adverse drug reactions in A tertiary Care Hospital in patients. ~ 277 ~ The Pharma Innovation Journal [Internet]. 2019;8(2):277-86.
24. Sundaran S, Udayan A, Hareendranath K, Eliyas B, Ganesan B, Hassan A, *et al.* Study on the classification, causality, preventability and severity of adverse drug reaction using spontaneous reporting system in hospitalized patients. Pharmacy (Basel). 2018;6(4):108. doi: 10.3390/pharmacy6040108, PMID 30274320.
25. Ali Kareem S, Belagodu Sridhar S. Shetty ms. Intensive monitoring of adverse drug reactions in nephrology unit of tertiary care teaching hospital [internet]. Saudi J Kidney Dis Transplant. 2019;30. Available from: Http://Www.Sjkdt.Org.
26. Priyanka PD, Vithya T, Hiremath SRR, Prasad S. Incidence and assessment of adverse drug reactions at A tertiary Care Hospital. J Pharm Pract Community Med. 2020;6(1):15-7. doi: 10.5530/jppcm.2020.1.5.
27. James J, Rani J. A prospective study of adverse drug reactions in A tertiary Care Hospital in South India. Asian J Pharm Clin Res. 2019:89-92.
28. Yadesa TM, Kitutu FE, Tamukong R, Alele PE. Yadesa Tm, Kitutu fe, Tamukong R, Alele Pe. Development and validation of 'prediction of adverse drug reactions in older inpatients (Padroi)' risk assessment tool. Clin Interv Aging. 2022;17:195-210. doi: 10.2147/CIA.S350500, PMID 35241911.
29. Puvvada RK, Undela K, P B S, Kuruvilla AV, Gupta BS. Knowledge and perception of pharmacy practice students on causality assessment of adverse drug reactions. Adv Pharmacol Pharm. 2021;9(4):94-9. doi: 10.13189/app.2021.090403.
30. Verbič MD, Brvar M, Kos MK. Adverse drug reactions in the ambulatory internal patients at the emergency department: focus on causality assessment and drug-drug interactions. Acta Pharm. 2023;73(2):195-210. doi: 10.2478/Acph-2023-0013, PMID 37307369.
31. Alenzi KA, Alanazi NS, Almalki M, Alomrani H, Alatawi FO. The evaluation of adverse drug reactions in Saudi Arabia: A retrospective observational study. Saudi Pharm J. 2022;30(6):735-41. doi: 10.1016/j.jsps.2022.03.018, PMID 35812140.
32. Murali M, Suppes SL, Feldman K, Goldman JL. Utilization of the Naranjo scale to evaluate adverse drug reactions at A free-standing children's hospital. PLOS ONE. 2021;16(1). doi: 10.1371/journal.pone.0245368.
33. Nimron K. A retrospective study on adverse drug reactions monitoring and reporting in A Quaternary Care Super Speciality Hospital in Karnataka. Asian J Pharm Pharmacol. G.K P Natasha J, N. S. 2022;8(5):144-8.
34. Le B, Aj N, Kirkham Jj, Peak M, Arnott J, Rl S, *et al.* Development of the Liverpool adverse drug reaction avoidability assessment tool. PLOS ONE. 2017;12(1).
35. Da Costa Lima E, De Barros Fernandes T, Freitas A, De Lima Sias JF, Land MGP, Aires MT, *et al.* Translation, transcultural adaptation and validation to Brazilian Portuguese of tools for adverse drug reaction assessment in children. BMC Med Res Methodol. 2021;21(1):141. doi: 10.1186/s12874-021-01315-9, PMID 34238235.
36. Roberts EK, Hawcutt DB, Turner MA. Prospective identification and causality evaluation of suspected adverse drug reactions in neonates. Br J Clin Pharmacol. 2021;87(3):1541-6. doi: 10.1111/bcp.14485, PMID 32696451.
37. Mouton JP, Mehta U, Rossiter DP, Maartens G, Cohen K. Interrater agreement of two adverse drug reaction causality assessment methods: A randomised comparison of the Liverpool adverse drug reaction causality assessment tool and the World Health Organization-Uppsala Monitoring Centre system. PLOS ONE. 2017;12(2):e0172830. doi: 10.1371/journal.pone.0172830, PMID 28235001.
38. Commentaire [internet]. Available from: http://Www.Cma.Ca/Cmaj/Vol-163/Issue-.
39. Shi X, Zuo C, Yu L, Lao D, Li X, Xu Q, *et al.* Real-world data of tigecycline-associated drug-induced liver injury among patients in China: A 3-year retrospective study as assessed by the updated Rucam. Front Pharmacol. 2021;12. doi: 10.3389/fphar.2021.761167.
40. Awortwe C, Makiwane M, Reuter H, Muller C, Louw J, Rosenkranz B. Critical evaluation of causality assessment of herb–drug interactions in patients. Br J Clin Pharmacol. 2018;84(4):679-93. doi: 10.1111/bcp.13490, PMID 29363155.
41. Anthony L, P P. Patterns, causality, severity, and preventability of adverse drug reactions: an observational study at A tertiary health-care center. Natl J Physiol Pharm Pharmacol. 2022;12(12):1. doi: 10.5455/njppp.2022.12.104912022021102022.
42. Petrova G, Stoimenova A, Dimitrova M, Kamusheva M, Petrova D, Georgiev O. Assessment of the expectancy, seriousness and severity of adverse drug reactions reported for chronic obstructive pulmonary disease therapy. SAGE Open Med. 2017;5:2050312117690404. doi: 10.1177/2050312117690404, PMID 28228952.
43. Mammen SJ. A study of adverse drug reactions in A tertiary care hospital of Pune. Pharmatutor. 2018;6(8):38. doi: 10.29161/PT.v6.i8.2018.38.

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