

Title: Adverse Drug Events and Medication Errors in African Hospitals: A Systematic Review

Journal name: *Drugs–Real World Outcomes*

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Appendix 1: Medline search strategy

1st concept - terms related to medication errors and adverse drug events
1. medication errors.mp.
2. exp Medication Errors/
3. exp Medication Systems, Hospital/
4. exp "Drug-Related Side Effects and Adverse Reactions"/
5. medication safety.mp.
6. prescribing errors.mp.
7. exp Pharmacy Service, Hospital/
8. exp Drug Prescriptions/
9. dispensing errors.mp.
10. transcribing errors.mp.
11. exp Nursing Staff, Hospital/ or administration errors.mp.
12. medication history.mp.
13. exp Medical History Taking/
14. medication errors.ti.
15. prescribing errors.ti.
16. dispensing errors.ti.
17. administration errors.ti.
18. adverse drug reactions.ti.
19. adverse drug events.ti.
2nd concept - terms describing hospital setting
20. exp Hospitals/
21. exp Hospitalization/
22. hospitalization.mp.
23. exp Patient Admission/
24. admission.mp.
25. exp Patient Discharge/
26. discharge.mp.

3rd concept - describing African regions
27. exp Africa, Western/
28. exp Africa, Northern/
29. exp South Africa/
30. exp Africa, Southern/
31. exp Africa, Eastern/
32. exp Africa, Central/
33. exp "Africa South of the Sahara"/
34. Africa.mp.

The search terms used in each key concept were combined using the OR Boolean operator, and then all the 3 key concepts were connected using the 'AND' operator. Broadly, this searching strategy was similar between databases.

S2 Appendix: Excluded articles with reasons

ADE/ADRs reports from single disease/agents

1. Abah IO, Akanbi M, Abah ME, Finangwai AI, Dady CW, Falang KD, et al. Incidence and predictors of adverse drug events in an African cohort of HIV-infected adults treated with efavirenz. *Germes*. 2015; 5(3):83-91.
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3. Adeyemi A, Adesola O, Olaogun O. Risk factors for virologic failure and adverse reactions among patients on triple antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*. 2009; 51:125.
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12. Kiguba R, Ononge S, Karamagi C, Bird SM. Herbal medicine use and linked suspected adverse drug reactions in a prospective cohort of Ugandan inpatients. *BMC complementary and alternative medicine*. 2016; 16:145.
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14. Lartey M, Asante-Quashie A, Essel A, Kenu E, Ganu V, Neequaye A. Adverse drug reactions to antiretroviral therapy during the early art period at a tertiary hospital in Ghana. *Pan Afr Med J*. 2014; 18(25).
15. Lorent N, Sebatunzi O, Mukeshimana G, Van den Ende J, Clerinx J. Incidence and risk factors of serious adverse events during antituberculous treatment in Rwanda: a prospective cohort study. *PloS ONE*. 2011; 6(5):e19566.

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Studies assessing ADR reporting (KAP studies)

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Non-relevant outcome

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Conference abstract

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Non-English

1. Amor M, Bensghir M, Belkhadir Z, Ghannam A, Azendour H, Drissi Kamili N, et al. [Medication errors in anesthesia: a Moroccan university hospitals survey]. *Annales francaises d'anesthesie et de reanimation*. 2012;31(11):863-9.
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Commentaries

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2. Oshikoya KA. Adverse event monitoring of artemisinin combination therapy in Nigeria: the challenges and limitations of the study. *West Afr J Med.* 2010;29(4):221–4.
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Non-African setup

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Review

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S3 Appendix: Methodological quality assessment

A. Methodological quality assessment for ADE studies

	Aderemi-Williams 2015 [30]	Benkirane 2009 [31]	Benkirane 2009 [78]	Cooke 1985 [32]	Dedefo 2016 [79]	Eshetie 2015 [33]	Jennane 2011 [80]	Kiguba 2017 [34]	Letaief 2010 [35]	Mabadeje 1979 [35]
Study design										
Was the study design clear (prospective, retrospective, combined)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Methods for identifying ADEs										
Were the methods used to identify ADEs described in sufficient detail?	N	Y	Y	N	Y	Y	Y	Y	N	Y
Were data collection methods (case-record review, medication chart review and laboratory data) clearly described?	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y
Were the individuals (physicians, pharmacists, nurses) who identifies ADEs clearly described?	N	Y	Y	NR	N	Y	Y	Y	Y	N
Methods for determining the causality										
Was the process of establishing the casual relationship described in detail?	N	Y	N	Unclear	N	Y	N	Y	Y	NR
Were standard methods (validated tool) used in the assessment?	N	N	Y	Y	N	Y	N	Y	Y	NR
Methods for determining preventability										
Was the assessment process of establishing preventability described in detail?	NR	N	N	NR	Y	Y	N	Y	N	NR
Were standard methods (validated tool) used in the assessment?		Y	N	NR	Y	Y	N	Y	Y	NR
Methods for determining severity										
Was the assessment process of establishing predictability described in detail?	NR	N	Y	NR	Y	Y	Y	Y	N	NR
Were standard methods (validated tool) used in the assessment?	NR	Y	Y	NR	Y	Y	Y	Y	Y	NR
Total	2	7	7	2	7	10	6	10	7	3

Abbreviation: Y, yes; N, no; NR, not reported

Methodological quality assessment for ADE studies (Cont'd)

	Matsaseng et al 2005 [37]	Mehta 2008 [38]	Mouton 2015 [39]	Mouton 2016 [40]	Oshikoya 2011 [42]	Tipping 2006 [43]	Tumwikirize 2011 [44]	Oshikoya 2007 [41]
Study design								
Was the study design clear (prospective, retrospective, combined)?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for identifying ADEs								
Were the methods used to identify ADEs described in sufficient detail?	N	N	Y	Y	Y	N	Y	Y
Were data collection methods (case-record review, medication chart review and laboratory data) clearly described?	Y	Y	Y	Y	Y	N	Y	Y
Were the individuals (physicians, pharmacists, nurses) who identifies ADEs clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for determining the causality								
Was the process of establishing the casual relationship described in detail?	Y	Y	Y	Y	Y	N	N	Y
Were standard methods (validated tool) used in the assessment?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for determining preventability								
Was the assessment process of establishing preventability described in detail?	NR	Y	Y	Y	Y	NR	N	N
Were standard methods (validated tool) used in the assessment?	Y	Y	Y	Y	Y	NR	Y	N
Methods for determining severity								
Was the assessment process of establishing predictability described in detail?	NR	Y	N	Y	Y	NR	N	NR
Were standard methods (validated tool) used in the assessment?	Y	Y	N	Y	Y	NR	Y	NR
total	7	9	8	10	10	3	7	6

Abbreviation: Y, yes; N, no; NR, not reported

B. Methodological quality assessment: MEs

	Agalu 2011 [45]	Agalu 2012 [58]	Ajemigbitse 2016 [49]	Ajemigbitse 2013 [46]	Ajemigbitse 2013 [47]	Ajemigbitse 2014 [48]	Alagha 2011 [50]	Arulogun 2011 [51]	Oshikoya 2007 [52]	Sada 2015 [53]	Yinusa 2004 [54]
Aims/objectives of the study clearly stated.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Definition of what constitutes a medication error.	Y	N	N	Y	N	Y	Y	Y	Unclear	Y	N
Error categories specified.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Error categories defined.	Y	N	N	Y	N	Y	Y	N	N	Y	N
Presence of a clearly defined denominator.	Y	Y	Y	Y	N	N	Y	Y	Unclear	N	Unclear
Data collection method described clearly.	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N
Setting in which study conducted described.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	Y	N	N	N	Y	N	Y	N
Reliability measures	N	N	N	N	N	N	N	N	N	N	N
Measures in place to ensure that results are valid.	N	N	Y	N	N	N	N	N	N	N	N
Limitations of study listed.	Y	Y	Y	Y	Y	N	Y	N	N	Y	N
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N	N
Ethical approval.	Y	Y	Y	Y	Y	Y	N	N	N	Y	N
Total	9	7	7	10	6	7	8	7	4	9	3

Abbreviation: Y, yes; N, no;

Methodological quality assessment: MEs (Cont'd)

	Yousif 2011 [55]	Zelege 2014 [56]	Amucheazi 2009 [61]	Gordon 2004 [63]	Gordon 2006 [64]	Feleke 2010 [65]	Feleke 2015 [66]	Labuschagne 2011 [67]	Llewellyn 2009 [68]	Agu 2014 [71]	al Tehewy 2016 [59]
Aims/objectives of the study clearly stated.	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y
Definition of what constitutes a medication error.	N	Y	N	N	N	Y	Y	N	Y	Y	Y
Error categories specified.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Error categories defined.	N	Y	N	N	N	Y	Y	N	N	N	N
Presence of a clearly defined denominator.	Y	N	Y	Unclear	Unclear	Y	N	Unclear	Y	Y	Y
Data collection method described clearly.	Y	Y	N	N	N	Y	N	Y	Y	Y	Y
Setting in which study conducted described.	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	N	N	N	Y	N	N	N	N
Reliability measures	N	N	N	N	N	N	Y	N	N	N	Y
Measures in place to ensure that results are valid.	N	N	N	N	N	N	N	N	N	Y	N
Limitations of study listed.	N	Y	N	N	Y	N	Y	N	N	Y	N
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N	N
Ethical approval.	N	Y	N	N	Y	N	Y	Y	Y	Y	Y
Total	5	8	2	3	5	7	8	5	7	8	8

Abbreviation: Y, yes; N, no

Methodological quality assessment: MEs (Cont'd)

	Benkirane 2009 [78]	Dedefo 2016 [79]	Negash 2013 [72]	Jennane 2011 [80]	Kandil 2012 [73]	Sabry 2014 [75]	Sabry 2009 [76]	Nwasor 2014 [69]	Oshikoya 2013 [70]	Shehata 2016 [77]
Aims/objectives of the study clearly stated.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Definition of what constitutes a medication error.	Y	Y	Y	Y	N	N	N	N	Y	N
Error categories specified.	N	Y	N	N	N	N	N	Y	Y	Y
Error categories defined.	N	Y	Y	N	Y	Y	N	N	N	N
Presence of a clearly defined denominator.	Y	Y	Unclear	Y	N	Y	N	Unclear	N	Y
Data collection method described clearly.	Y	Y	N	Y	N	Y	N	N	Y	Y
Setting in which study conducted described.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	N	N	N	N	N	N	N
Reliability measures	Y	Y	N	Y	N	N	N	N	N	N
Measures in place to ensure that results are valid.	Y	N	N	N	N	N	Y	N	Y	N
Limitations of study listed.	Y	Y	N	N	N	Y	Y	N	Y	Y
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N
Ethical approval.	N	Y	Y	Y	N	Y	N	N	Y	Y
Total	8	7	5	7	3	7	4	3	8	7

Abbreviation: Y, yes; N, no

Methodological quality assessment: MEs (Cont'd)

	Acheampong 2016 [57]	Amponsah 2016 [60]	Blignaut 2017 [62]	Ogunleye 2016 [74]	
Aims/objectives of the study clearly stated.	Y	N	Y	Y	
Definition of what constitutes a medication error.	Y	N	N	Y	
Error categories specified.	Y	N	Y	Y	
Error categories defined.	Y	N	N	N	
Presence of a clearly defined denominator.	Y	N	N	Y	
Data collection method described clearly.	Y	Y	Y	Y	
Setting in which study conducted described.	Y	N	Y	Y	
Sampling and calculation of sample size described.	N	N	Unclear	N	
Reliability measures	Y	N	Y	N	
Measures in place to ensure that results are valid.	Y	N	Y	N	
Limitations of study listed.	Y	N	Y	N	
Mention of any assumptions made.	Y	N	N	N	
Ethical approval.	Y	Y	Y	Y	
Total	12	2	8	7	

Abbreviation: Y, yes; N, no

S4 Appendix: Definition and assessment of ADEs and MEs

A. Definition and assessment of ADEs

Author, year	Definition and/or description of the incident	A person/ team responsible for identification	Further verification of ADEs	Person responsible for causality, severity and preventability assessment
Adverse drug events				
Aderemi-Williams 2015 [30]	NR	NR	NR	NR
Benkirane 2009 [31]	An injury resulting from medical interventions related to a drug (WHO definition)[26]	Medical residents	NR	Causality, 2 experienced investigators Severity, NR Preventability, NR
Benkirane 2009 [78]	Bates et al 1995 [25] ADE definition (ADRs and complications from MEs)	Pharmacists investigators		Two reviewers of the pharmacovigilance centre staffs evaluated causality and severity Preventability: NR
Cooke 1985 [32]	Any undesired or unintended effect of drugs	NR	NR	NR
Eshetie 2015 [33]	Any incident resulting in injury from any stage of the medication use process (ordering, transcribing, dispensing, administrating and monitoring)	Multidisciplinary	Pediatrics team	Causality: clinical pharmacist Severity and preventability: two senior pediatric residents
Dedefo 2016 [79]	An ADE refers to all ADRs, including allergic or idiosyncratic reactions, as well as MEs that result in harm to a patient	Pharmacist researcher	NR	Severity and preventability: one pediatrician and one clinical pharmacist
Jennane 2011 [80]	Any injury resulting from medical interventions related to a drug	A pharmacist and a physician	NR	Causality, NR Severity: Physician reviewers rated the severity of ADEs Preventability, NR

Kiguba 2017 [34]	WHO definition of ADR [85]	A medical doctor, pharmacist and degree nurse	Study physicians (gynecologist/obstetrician, internist) and research pharmacist (senior clinical pharmacist)	Consensus agreement on ADR causality, preventability, severity and seriousness was reached in a committee headed by the ward-based study physician and senior clinical pharmacist
Letaief 2010 [35]	Injury related to medical management in contrast to complications of the disease	Medical student	2 expert physicians	NR
Mabadeje 1979 [36]	NR	NR	NR	NR
Matsaseng 2005 [37]	An injury that was caused by medical management (rather than the underlying disease)	Researcher	Supervising specialist	NR
Mehta 2008 [38]	WHO definition of ADR [89]	Clinical pharmacology team	Clinical pharmacist, 4 clinical pharmacology registrars and a hospital pharmacist	2 clinical pharmacology consultants assess cases for causality, severity and preventability
Mouton 2015 [39]	ADR according to the definition of Aronson and Ferner ^a	Clinical pharmacologist	Clinical pharmacologist, clinical pharmacist, at least 1 physician/internist	A multidisciplinary review panel assessed ADRs for causality and preventability
Mouton 2016 [40]	ADR according to the definition of Aronson and Ferner ^a	One medical doctor and 2 pharmacists	Multidisciplinary panel discussion	A multidisciplinary case review panel assessed ADRs for causality, preventability, and severity
Oshikoya 2007 [41]	WHO definition of ADR [26]	Clinical pharmacologist, pediatrician, pharmacist	Pharmacists, pharmacologist, pediatric dermatologist	NR
Oshikoya 2011 [42]	WHO definition of ADR [26]	A pediatric clinical pharmacologist,	NR	The pediatric clinical pharmacologist and one of the two pharmacists assess the

		pediatricians, ² hospital pharmacists		suspected ADRs for causality, severity and preventability independently
Tipping 2006 [43]	ADEs, as defined by the South African Medicines Formulary	Primary physician and/or the principal investigator	NR	NR
Tumwikirize 2011[44]	WHO definition of ADR [89]	A physician and a pharmacist	NR	NR

NR, Not reported

^aAronson JK, Ferner RE. Clarification of terminology in drug safety. Drug Saf 2005; 28:851-70.

B. Definition and assessment of MEs

Author, year	Definition and/or description of the incident	Person/team assessing the clinical significance
Prescribing errors		
Agalu 2011 [45]	Prescribing error implies deviation of medication prescribing from standard practices excluding dosage form errors, illegible hand writing, and failure to authenticate the prescription with signature and/or date	NR
Ajemigbitse 2016 [49]	NR	NR
Ajemigbitse 2013 [46]	Any deviation from a complete, accurate and legible prescription, as it pertains to errors on the prescription and not the prescribing decision or dispensed medicines	3 clinical pharmacists
Ajemigbitse 2014 [48]	NR	NR
Ajemigbitse 2013 [47]	A prescribing decision or prescription writing process that results in an unintentional, significant reduction in the probability of treatment being timely and effective or increases the risk of harm when compared with generally accepted practice	NR
Alagha 2011 [50]	An error that occurs at the stage of prescribing excluding date of order and signature of the prescriber	A clinical pharmacist and a consultant pediatrician
Arulogun 2011 [51]	Prescriptions were evaluated for legality (name of patient, date, prescription number, signature) and for other types of error such as dose, duration, illegible writing	NR
Oshikoya 2007 [52]	NR	NR
Sada 2015 [53]	Prescribing error: deviation of medication prescribing from standard practices (as indicated in standard treatment guidelines, textbooks, and software) excluding, indication without drug, dosage form errors, illegible	The principal investigator and 1 internist

	hand writing, and failure to authenticate the prescription with signature and/or date.	
Yinusa 2004 [54]	All prescription items which did not conform to the criteria for prescription writing as stated in the British National formulary	NR
Yousif 2011 [55]	Neville et al [97] definition of prescribing errors	NR
Zelege 2014 [56]	Deviation of medication prescribing from standard practices and includes inappropriate (incorrect) drug selection, wrong dose, wrong frequency, wrong route and wrong dosage form	NR
Medication administration errors		
Acheampong 2016 [57]	An administration error is said to be occurred when what was administered is different from what had been prescribed.	2 clinical pharmacists
Agalu 2012 [58]	Deviation from the conventional method of administration of a particular drug as ordered by the prescribing physician	NR
al Tehewy 2016 [59]	A deviation from a prescriber's valid prescription or the hospital's policy in relation to drug administration, including failure to correctly document the administration of a medication.	NR
Amponsah 2016 [60]	NR	Self-report
Amucheazi 2009 [61]	NR	NR
Blignaut 2017 [62]	NR	NR
Gordon 2004 [63]	Wrong drug administrations or the right drug into the wrong site	Self-report
Gordon 2006 [64]	Wrong drug administrations	Self-report
Feleke 2010 [65]	A medication error that occurs while administering a medication to a patient including unauthorized use of medicines	NR
Feleke 2015 [66]	Medication administration error: A medication error (time, dose, missed drug, unauthorized, route, technique, and documentation errors) that occurs while the time of	NR

	administering IV, IM, SC, and PO medication to the patient by the nurse	
Labuschagne 2011 [67]	NR	Self-report
Llewellyn 2009 [68]	NR	Self-report
Nwasor 2014 [69]	NR	Self-report
Oshikoya 2013 [70]	Wrong medicine dose measurement, administration of wrong medicines, wrong patient, wrong route of administration, wrong timing and speed of administration, and omission of medications	NR
Medication errors (Mixed)		
Agu 2014 [71]	NR	NR
Dedefo 2016 [79]	NR	NR
Benkirane 2009 [78]	Adopted from NCCMERP [24]	2 reviewers of the pharmacovigilance center
Negash 2013 [72]	Adopted from ASHP ^b	NR
Jennane 2011[80]	Adopted from NCCMERP [24]	2 physician evaluators
Kandil 2012 [73]	Administration error: a medication error that occurred while administering a medication to a patient including unauthorized error, Prescription error: a failure in the prescription writing process that resulted in a wrong instruction	NR
Ogunleye 2016 [74]	Any error in prescribing, dispensing, or administration of drugs, irrespective of whether such errors lead to adverse consequences or not	NR
Sabry 2014 [75]	Prescribing errors, adopted from Anderson 2003; Administration errors, any deviation from the physician's medication order as written on the patient's chart including timing problems, missing doses as observed from the administration sheet and after confirming with the nurse, an extra dose as observed from the quantities of unit doses remaining in the patient's tray, or wrong infusion flow rate	NR

Sabry 2009 [76]	Any problems connected with medications prescribed to the enrolled patients	NR
Shehata 2016 [77]	Adopted from NCCMERP [24]	NR

NR, not reported

^b ASHP guidelines on preventing medication errors in hospitals. Am J Hosp Pharm 1993; 50:305-14.