



Medication Safety Newsletter

Inside...

Glossary	2
A quick look on NOHARMe data	3
Aspirin: An old known drug	9
References	12

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Drug Utilization and Pharmacy Practice Administration is pleased to publish its medication safety newsletter.

The medication safety newsletter was launched to provide information on the safe and effective use of medications and to share information on the patterns of medication errors and drug therapy problems reported to the NOHARMe system. In appreciation for their efforts, we would like to thank all clinical pharmacists who have been keen on documenting their interventions during the pandemic period.

Our Vision

To be the leader in the middle east towards high quality pharmaceutical care services with optimal drug utilization that is based on evidence and matches with international systems.

Glossary

NOHARMe	National Office for Handling AND Reducing Medication Errors
DTP	Drug Therapy Problem
ME	Medication Error
ACS	Acute Coronary Syndrome
AHA	American Heart Association
ACC	American College of Cardiology
STEMI	ST-Segment Elevation Myocardial Infarction
NSTEMI	Non-ST-Segment Elevation Myocardial Infarction
ESC	European Society of Cardiology
DAPT	Dual Antiplatelet Therapy
PCI	Percutaneous Coronary Intervention
AIS	Acute Ischemic Stroke
CHA2DS2-VASc	Congestive heart failure, Hypertension, Age, Diabetes, Stroke,
VKA	Vascular disease score
IHD	Vitamin-K Antagonist
ASCVD	Ischemic Heart Disease
ADA	Atherosclerotic Vascular Disease
HAS-BLED	American Diabetes Association
AF	Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INR, Elderly, Drugs or alcohol bleeding score

A quick Look on NOHARMe Data Collected over 6 Months

Overall numbers

A total of 16,326 reports have been generated in 6 months, 32.33% of which have been labelled as drug therapy problems “DTPs”, 7.10% have been labelled as medication errors “MEs”, and 60.57% have been labelled as drug therapy problem that are also medication errors.

Report Type	(%)
Drug Therapy Problems (DTPs)	32.33%
Medication Errors (MEs)	7.10%
DTPs that are also MEs	60.57%

Analysis of the Drug Therapy Problems:

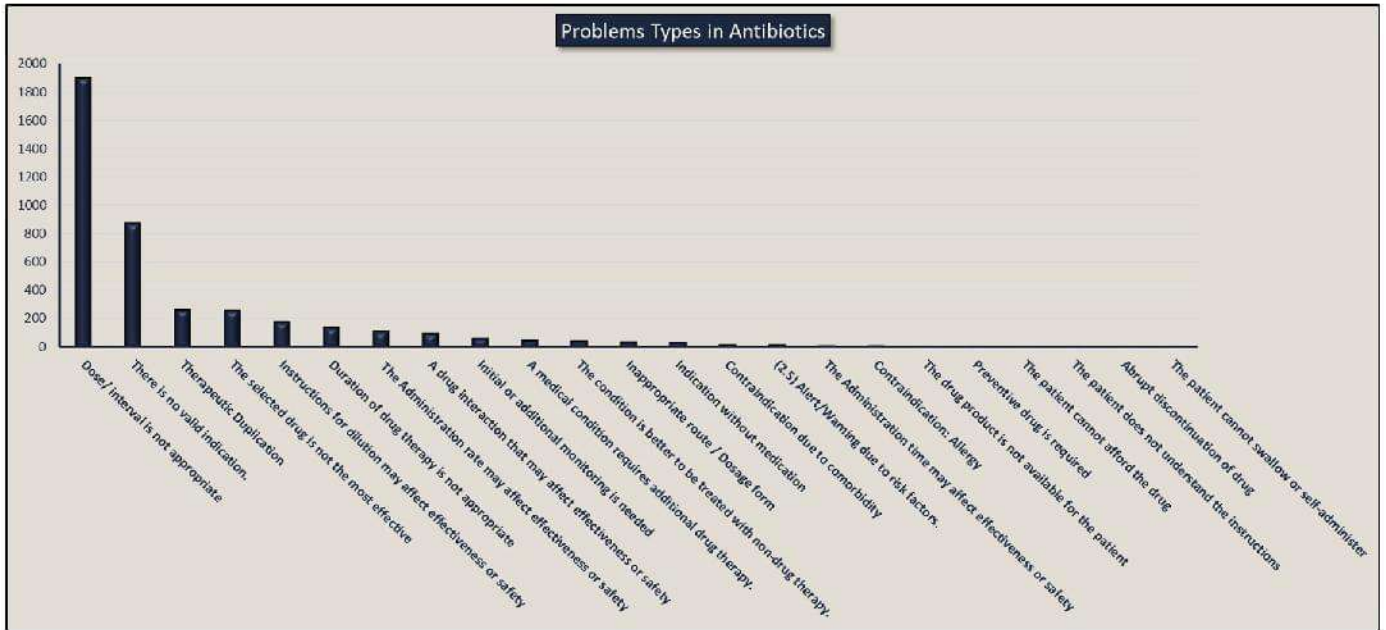
The drug therapy problems referred to here include reports labeled as DTPs in addition to the reports labeled as DTPs and MEs also. 343 unique scientific drug names have been used in all the reports, the top 58 most used drugs roughly account for about 80% of all the reports. It is important to note that “None (No drug)” is used to reports DTPs in which drugs are needed to be added to the medical treatment. Those

drugs also include antibiotics, anticoagulants, antiplatelets, drugs for lowering gastric pH, corticosteroids, and other drugs including drugs used for chronic conditions e.g., drugs for CVS, CKD, antiepileptics. In this analysis we will attempt to look at each group of drugs separately.

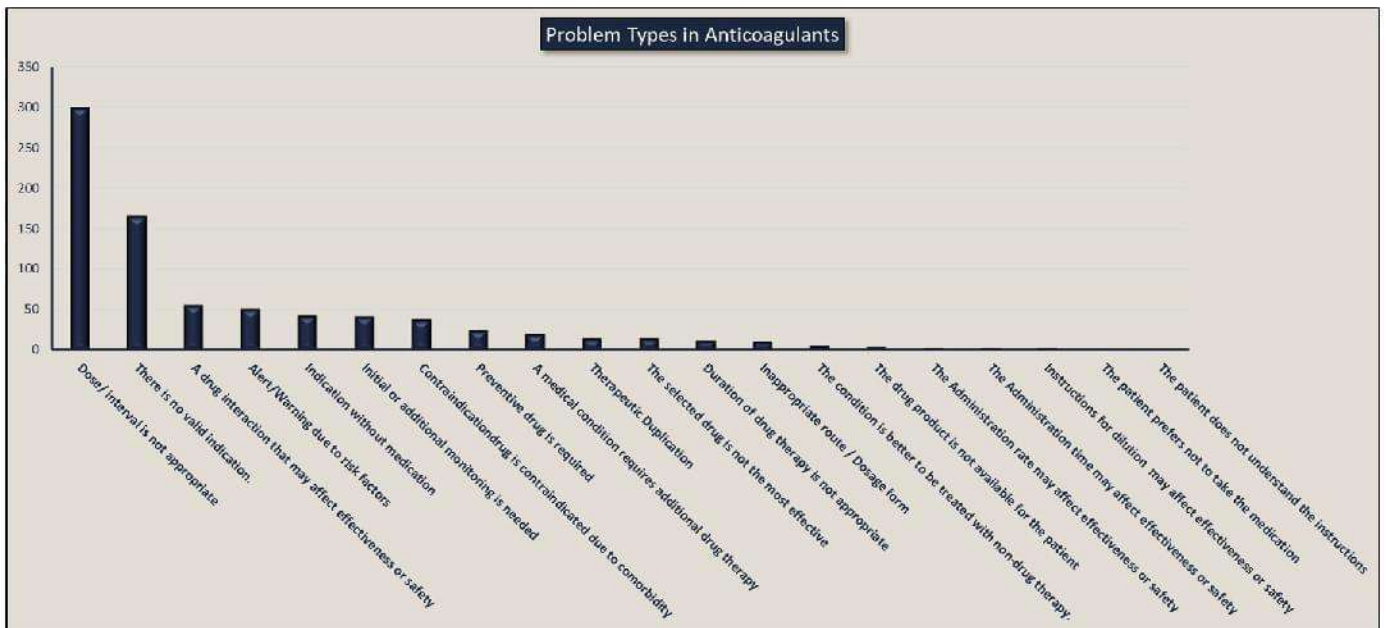
The following charts show the most common types of problems reported for each group of drugs:

- Problem types in antibiotics.
- Problem types in drugs used for acid reflux.
- Problem types in corticosteroids.
- Problem types in drugs used for chronic conditions.

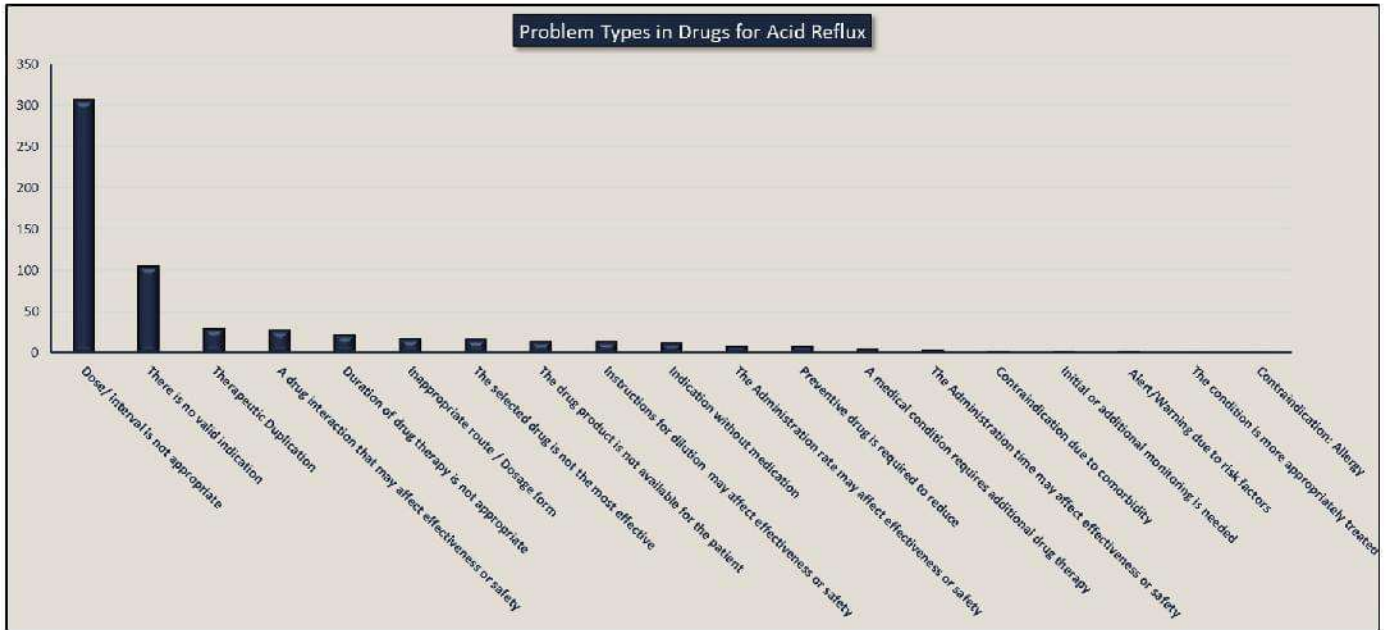
Problem Types in Antibiotics



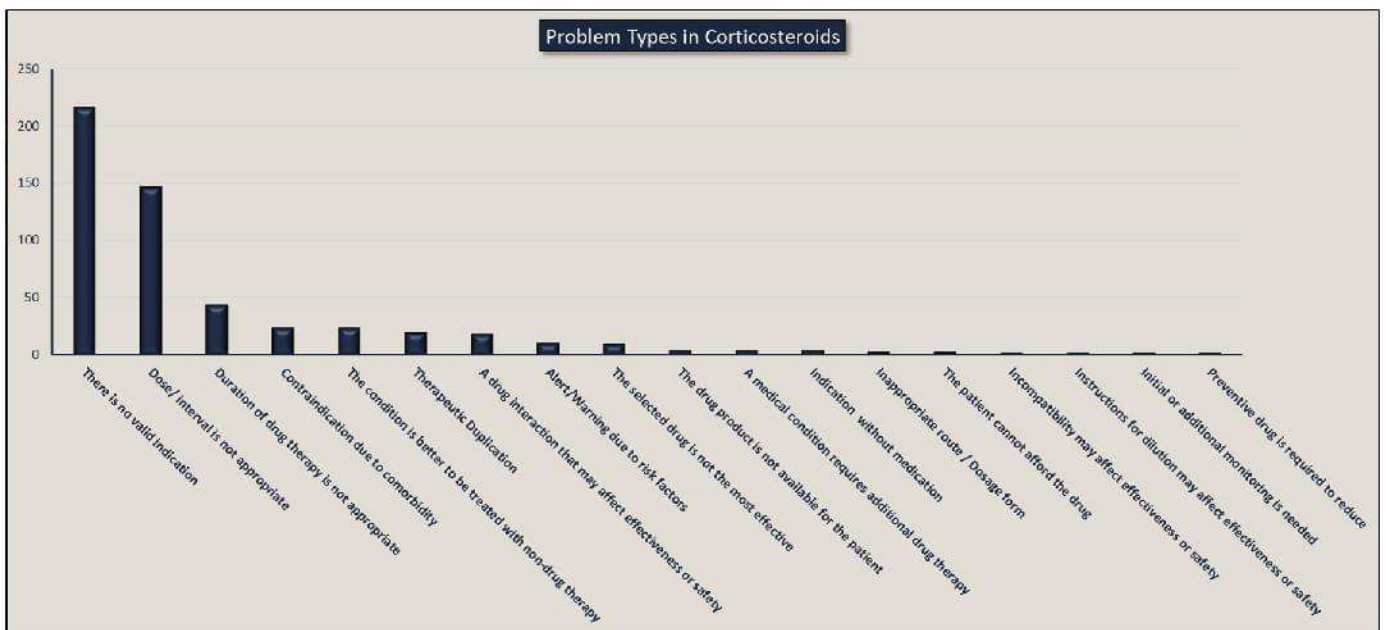
Problem Types in Anticoagulants



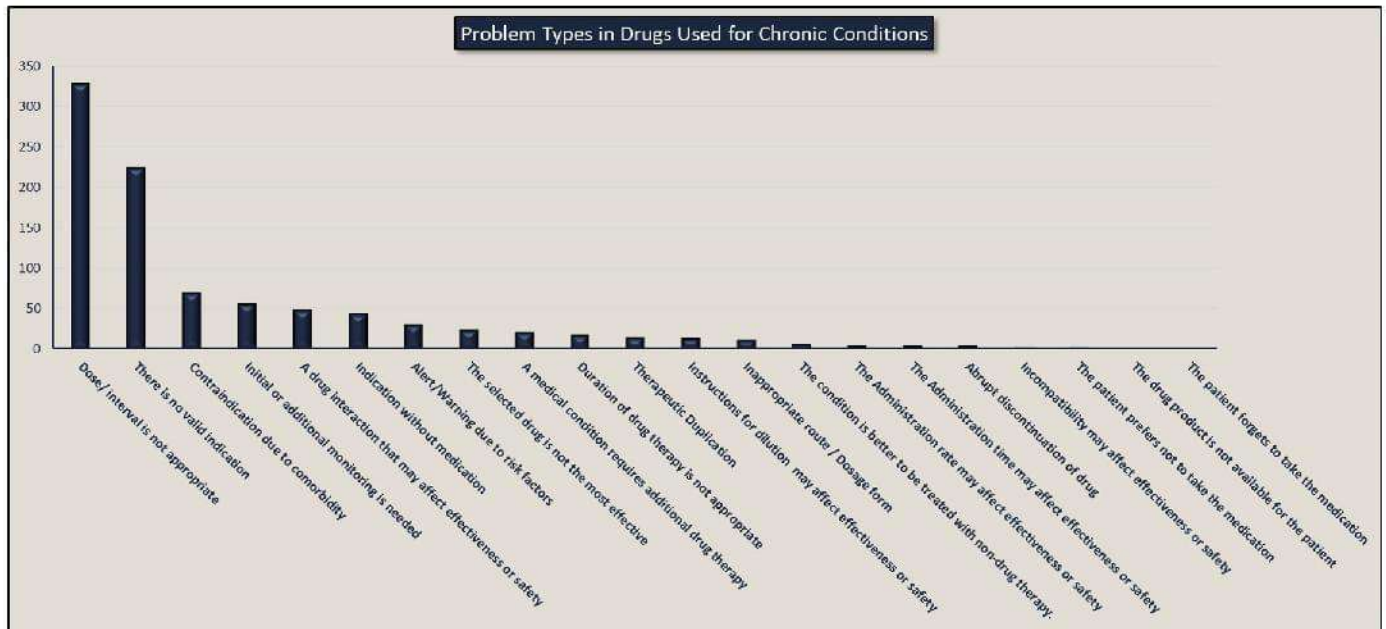
Problem Types in Drugs Used for Acid Reflux



Problem Types in Corticosteroids



Problem Types in Drugs Used for Chronic Conditions



Drug Interactions:

A total of 203 drug-drug interactions have been reported. The most significant interactions were:

- Amiodarone and levofloxacin: Each drug on its own prolongs the duration of the QTc interval and their concurrent use increases the risk for torsades de pointes.
- Amiodarone and clarithromycin: Similar to the previous interaction, the concurrent use of both drugs increases the risk of torsade de pointes. Torsades de pointes can be fatal and may cause death by sudden cardiac arrest thus; amiodarone should not be used with either clarithromycin or levofloxacin.

recommendations is good overall with an average rate for acceptance of 72.93% of the grand total.

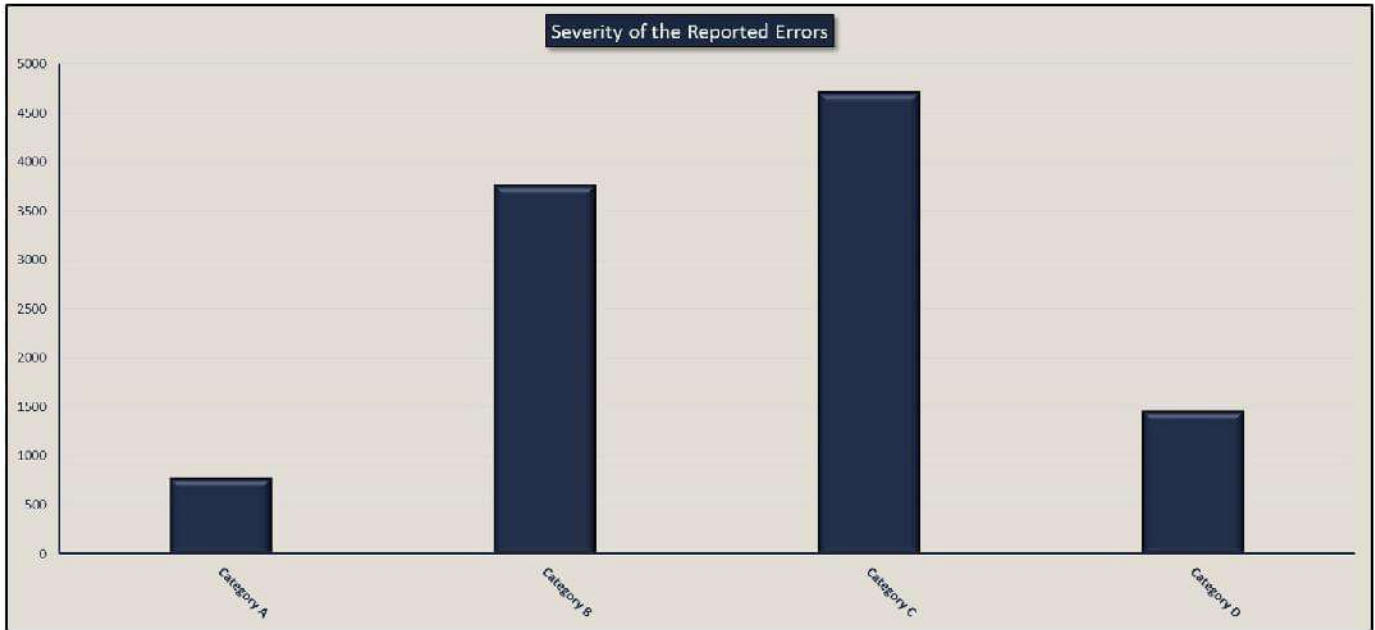
Analysis of the Reported Medication Errors

Medication errors are any event or condition that leads to inappropriate medication use while the medication is under the control of either the medical staff, patients or their caregivers. In NOHARME, MEs are categorized according to the stage of medication use cycle in which the error occurs. The following graphs depict the severity, stages and causes of reported errors.

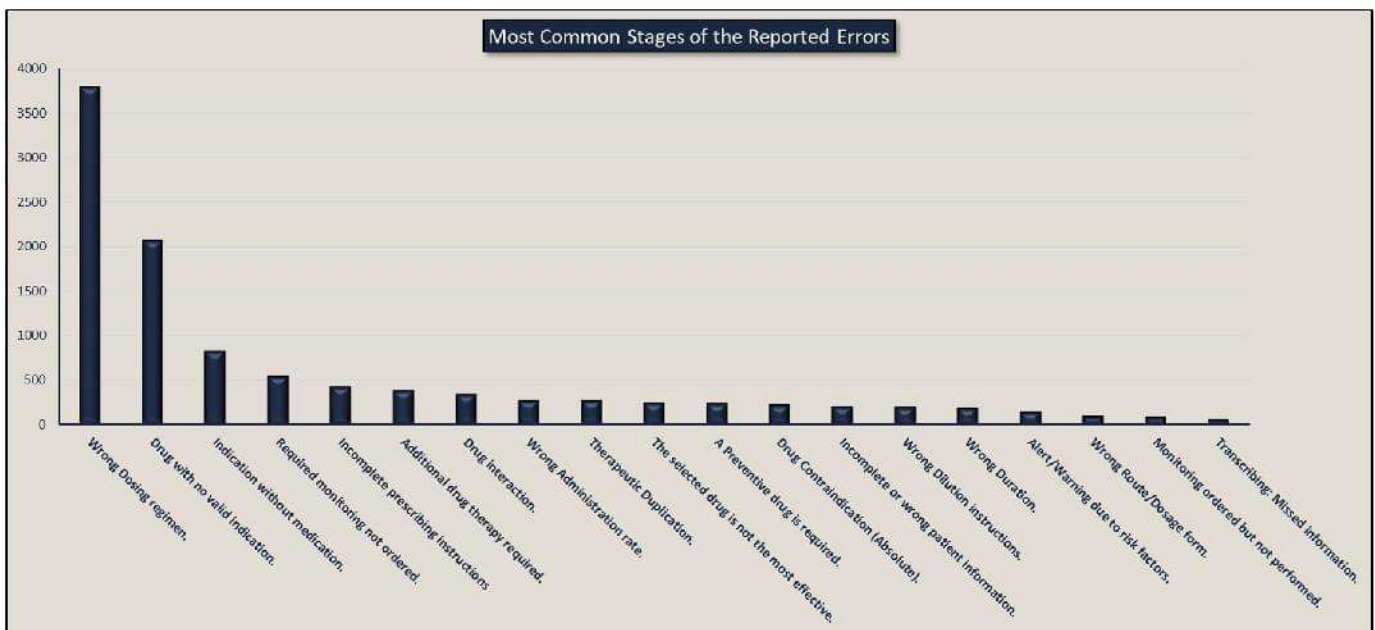
Acceptance Rates of clinical pharmacy interventions across all direcotrates:

Physician acceptance of the clinical pharmacist

Severity of the reported errors

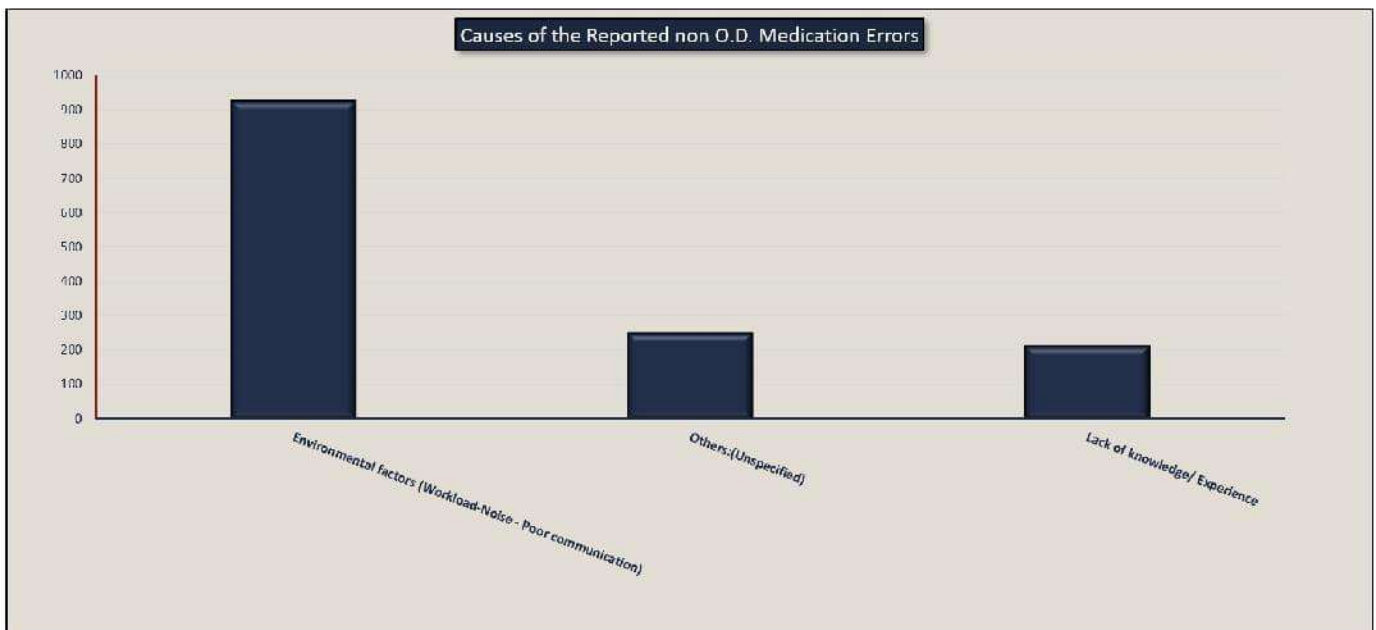
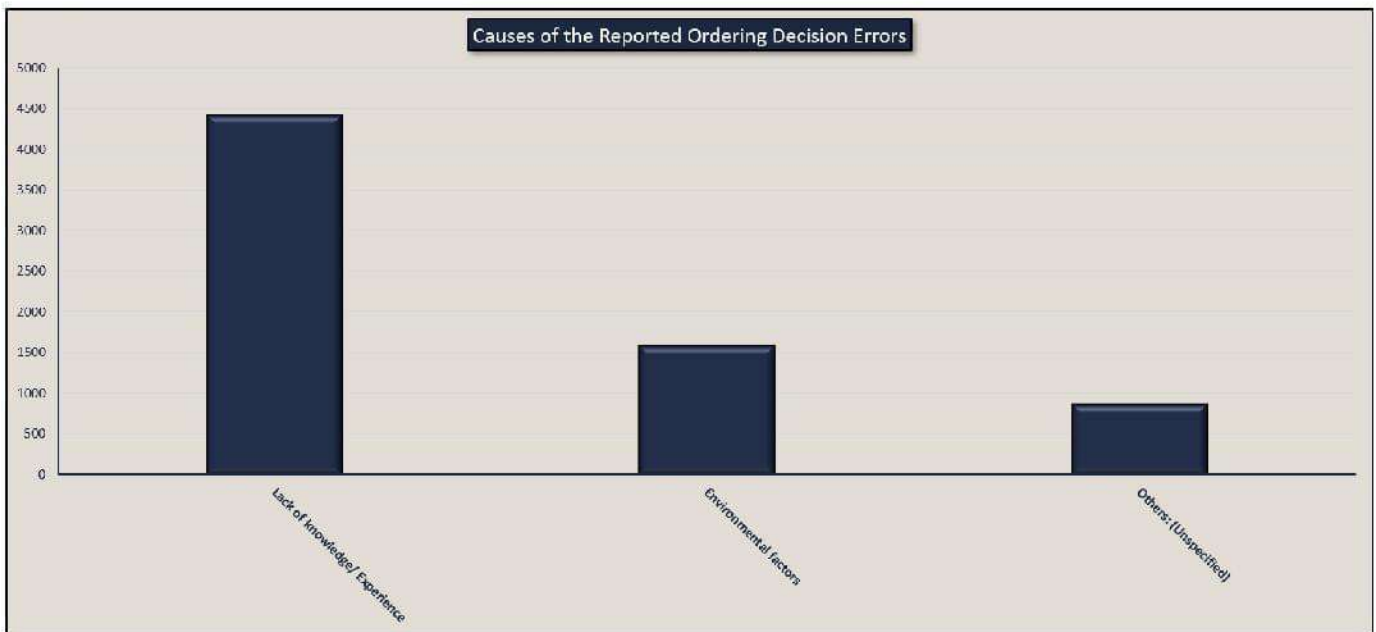


Errors by stages of the medication use cycle



Causes of errors

Ordering-decision errors are errors that were reported initially as drug therapy problems then documented as medication error because physicians lacked information about either the patients they were treating or the medications they were prescribing. Non-ordering-decision errors encompass all the errors that occur in one the medication use cycle stages and do not involve any decision making.



Aspirin, An Old Known Drug, It's Multiple Roles and The Updates



Data analysis of NOHARMe (data collected over 6 months):

Analysis of the drug therapy problems (DTPs) showed that 343 unique scientific drug names have been used in all the reports. Among those 343 drug, 58 drugs were on top as most associated with drug therapy problems. Aspirin was one of those 58 top drugs accounting for 232 DTPs reports. The top 5 reported problems associated with Aspirin were:

- 1- Dosing.
- 2- No Valid indication for the drug.
- 3- Drug Interactions.
- 4- Alert/Warning due to risk factor.
- 5- Indication without medication.

First, Regarding Aspirin Dosing problems ,The following problems were detected:

a. Aspirin Dosing in Acute Coronary Syndrome (ACS) : STEMI & NSTEMI-ACS: There is a difference between dosing recommendations in ACS according to American Heart Association/American College of Cardiology (AHA/ACC) guidelines and European Society of Cardiology (ESC) guidelines in both loading and maintenance doses:

- AHA/ACC Guidelines (2013 STEMI Guidelines , 2014 NSTEMI-ACS Guidelines): Aspirin Loading Dose : 162 - 325 mg, Maintenance Dose : 81 - 325 mg.
- ESC Guidelines(2017 STEMI Guidelines ,

2020 NSTEMI-ACS Guidelines) : Aspirin Loading Dose : 150 -300 mg, Maintenance Dose : 75 - 100 mg While if we looked at 2016 AHA/ACC guidelines on Dual Antiplatelet Therapy (DAPT) Therapy ,we shall find them stating that "Aspirin dosing recommendations across AHA/ACC clinical practice guidelines are not consistent with regard to dose or class of recommendation, and because aspirin is a component of DAPT, They made a larger review and recommended Lower Aspirin doses \leq 100 mg (whether monotherapy or combined with P2Y12 inhibitor Clopidogrel due to less major and total bleeding than higher doses) and specifically 75 - 100 mg daily in case of DAPT therapy.

- However Both ESC guidelines and AHA/ACC guidelines recommended Aspirin dose of 75 - 100 mg in case of a patient with mechanical valve using Warfarin and that the patient had an indication requiring addition of Aspirin.
- It is worth noting that Aspirin dose varies widely depending on the indication and patient complications; and it is important to take into consideration the occurrence of pericarditis as a complication of post myocardial infarction.
- Anti-inflammatory therapy is recommended in post-STEMI pericarditis as in post-cardiac injury pericardial syndromes for symptom relief and reduction of recurrences. Aspirin is recommended as first choice of anti-inflammatory therapy post-STEMI at a dose of 500-1000 mg every 6-8 h for 1-2 weeks, decreasing the total daily dose by 250-500mg every 1-2weeks as recommended by 2017 ESC guidelines While 2013 AHA/ACC Guidelines on STEMI recommended Aspirin



without recommending specific dose.

b. Aspirin Dosing in Acute Ischemic Stroke(AIS):

- 2019 American Heart Association / American Stroke Society Guidelines on early management of patients with acute ischemic stroke: No specific dosing recommendation.
- The recommendation was modified from the 2013 guidelines to remove the specific dosing.
- Recommendation: “initial dose is 325 mg” because previous clinical trials supporting its use for AIS included doses of 160 to 300 mg.

Second, Regarding errors detected as no valid indication for Aspirin,the following problems were reported:

a. Aspirin indication in AF:

There is a difference ESC and AHA guidelines on the use of Aspirin in AF Where: 2014 AHA/ACC/HRC guidelines on AF recommends either Aspirin with weak recommendation (IIb) and a level of evidence (C) in patients with non-valvular AF and a CHA2DS2-VASc score of 1 for stroke primary prevention. This point was not updated by a different recommendation in 2019 focused update of the guidelines. While 2020 ESC guidelines on AF doesn't recommend use of Aspirin for stroke primary prevention in patients with AF. Neither did the previous 2016 ESC guidelines.

b. Aspirin in case of Triple therapy:

Clinical pharmacists' reports highlighted a very important point which is the duration of Dual antiplatelet therapy of Aspirin and P2Y12 Inhibitor (clopidogrel) together with an oral anticoagulant. This situation requires careful review of patient data and assessment that must include the following:

- Diagnosis that patient admitted for (Whether Acute Coronary Syndrome Or another indication as presentation with Acute Heart Failure Syndrome on Stable Ischemic Heart disease background)

- Intervention done to patient (Percutaneous Coronary Intervention (PCI)or Thrombolytics for STEMI & Invasive Strategy or Medical management for NSTEMI-ACS)

- Patient Past Medication history as of Aspirin ,Clopidogrel or oral anticoagulant in terms of duration.

Indications for anticoagulation in a patient include:

- Assessment of both Thrombosis and bleeding risk using CHA2DS2-VASc and HAS-BLED scores in AF patients .

- All these factors determine whether Aspirin is indicated for patient or not at this point of time.

- This duration also shows variability in recommendation between AHA/ACC guidelines and ESC Guidelines .

- For example : 2020 ESC guidelines on AF changed recommendation of Triple therapy as to ≤ 1 week for ACS uncomplicated patient treated with PCI and has high bleeding risk prevailing over thrombosis risk and then to use P2Y12 inhibitor preferably Clopidogrel together with oral anticoagulant and discontinuing Aspirin (irrespective of stent type).Which is not the case if used AHA/ACC guidelines recommendations.

c. Aspirin indication in Valvular Heart disease:

- Clinical pharmacists highlighted an important issue which is the indication of Aspirin in patients with Mechanical Heart valves (Mechanical Prosthesis)

- Where 2020 AHA/ACC guidelines on Valvular Heart disease changed its recommendation regarding addition of Aspirin to VKA in patients with mechanical prosthesis that was previously stated in 2014 Guidelines to its addition only in case of other indication or in case of patients who experience a stroke or systemic embolic event while in therapeutic range on Vitamin K-Antagonist (VKA) anticoagulation.



• While 2017 ESC guidelines on Valvular Heart Diseases recommended addition of low dose Aspirin in patients with Mechanical prosthesis after thromboembolism despite an adequate INR.

Third, Regarding errors detected as indication without medication errors detected were highlighting 2 important issues:

a. Patients previously known as IHD patients and admitted for another reason than ACS leading to missing Aspirin in prescribed medication.

b. Use of Aspirin in primary prevention in hypertensive and diabetic patients: Clinical pharmacists in their reports highlighted a very important issue which is the use of Aspirin in primary prevention.

Guideline differences:

• 2016 ESC Guidelines on Cardiovascular disease prevention: Does not recommend the use of Antiplatelets in individuals without Cardio Vascular Disease (CVD) including diabetic patients.

• 2019 AHA/ACC guidelines on Primary Prevention of Cardiovascular Disease : recommended that low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of Atherosclerotic Cardiovascular diseases (ASCVD) among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk but with weak level of recommendation (IIb) and a level of evidence (A).

• 2021 ADA Guidelines Stated that : Aspirin therapy (75–162 mg/ day) may be considered as a primary prevention strategy in those with diabetes who are at increased cardiovascular risk, after a comprehensive discussion with the patient on the benefits versus the comparable increased risk of bleeding.

Analysis of all these Drug Therapy problems

reported by clinical pharmacists draw us to the following recommendation for best standardized clinical pharmacy practice:

1. Each hospital should develop a Local Antiplatelet Protocol for both inpatient and outpatient settings based on evidence based guidelines where recommendations with higher evidence are selected ,submitting this protocol to Drug and Therapeutic Committee and finally getting approval. This creates harmonization between clinical pharmacists and physicians in debate points in guidelines and provides standardization of practice.

2. Continually updating the protocol to cope with latest evidence.

3. Implementation of medication reconciliation system on admission, transfer and discharge that involves clinical pharmacists for accurate patient history taking.

References

- 2013 AHA/ACC guidelines on STEMI
- 2014 AHA/ACC Guidelines on NSTEMACS
- 2015 ESC Guidelines on NSTEMACS
- 2017 ESC Guidelines on STEMI
- 2014 AHA/ACC Guidelines on AF
- 2019 AHA/ACC Focused update of Guidelines on AF.
- 2020 ESC Guidelines on AF
- 2019 AHA/ASS Guidelines on AIS
- 2016 AHA/ACC Guidelines on DAPT Therapy.
- 2017 ESC Guidelines on DAPT Therapy
- 2017 ESC Guidelines on Valvular Heart Diseases.
- 2020 AHA/ACC Guidelines on Valvular Heart Diseases.
- 2020 ADA Guidelines on Diabetes Care
- 2021 ADA Guidelines on Diabetes Care
- 2016 ESC Guidelines On Cardiovascular disease prevention.
- 2019 AHA/ACC guidelines on Primary Prevention of Cardiovascular Disease.

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