

## **Expected Prescription Error (EPE) Scores of Cancer Drugs in Egypt: A New Method of Data Extraction from a Questionnaire Based Study**

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**Registration Details Of The Current Study:** The current study is a part of a research registered on [www.clinicaltrial.gov](http://www.clinicaltrial.gov) NCT02630979. The study received approval from the Institutional Review Board (IRB) of the Clinical Oncology department. Faculty of Medicine, Ain Shams University in October 2015.

**Sources Of Support:** There is no source of support of any type either financial or technical received by the authors of this study to implement this study. No source of funding from National Institutes of Health (NIH); Wellcome Trust; Howard Hughes Medical Institute (HHMI); or other(s).

### **Introduction:**

Many pharmaceutical aspects are crucial for cancer drugs efficacy as proper dosing schedules, medical contraindications, proper methods and timing of administration, proper preparations and storage procedures, drug interactions and dose relation to meals in oral drugs. Medication related errors were a significant cause of morbidity and mortality. Medication errors were estimated to account for more than 7000 deaths annually.<sup>(1)</sup>

Leape and colleagues reported more than 15 types of medication errors: wrong dose, wrong choice, wrong drug, known allergy, missed dose, wrong time, wrong frequency, wrong technique, drug-drug interactions, wrong route, extra dose, failure to act on test, equipment failure, inadequate monitoring, preparation error and others. The majority of physician's errors were wrong dose, wrong choice of drug and known allergy.<sup>(2)</sup> Tissot and Vanden Bernt examined only administartion stage errors and reported very different rates. Tissot reported 6.6 percent of the 2009 observed doses were in error, most from wrong dose, wrong rate and wrong preparation technique. Excluding wrong time error, Van den Bernt reported a 33 percent error rate that included preparation errors with diluent solvent issues, infusion rates errors and chemical incompatibility of intravenous drugs.<sup>(3,4)</sup>

In the field of chemotherapy, prescription errors may increase patient,s sufers either by increased toxicity or reduced efficacy. A systematic syrvey study reported by Ulas and colleagues stated that 83.4% of the 210 nurses reported one or more than one error during chemotherapy preparation and administration. Prescribing or ordering wrong doses by physicians (65.7%) and noncompliance with administration sequences during chemotherapy administration (50.5%) were the most common errors. The most common estimated average monthly error was not following the administration sequence of the chemotherapeutic agents (4.1times/month, range 1-20). The most important underlying reasons for medication errors were heavy workload (49.7%) and insufficient number of staff (36.5%).<sup>(5)</sup>

The aim of the current study is to propose potential approaches for optimization of the efficacy and minimization of the toxicities of cancer drugs in Egypt.

The study exposes the unintentional potentially pitfalls in the clinical practice of Egyptian medical and clinical oncologists by defining the preventable errors during prescription of medication, ordering, preparation or administration of expensive cancer drugs. The study is based on a systematic survey conducted to reflect medical oncologist's orientation with crucial pharmaceutical perspectives of expensive cancer drugs.

The end point of the study is to validate a questionnaire based scoring module called Expected Prescription Error (EPE) score. The drugs will be categorized in descending order accordingly. Teaching tutorials for the oncologists will be nationally implemented for the tested drugs with the high and intermediate EPE scores **aiming for improving the quality of cancer service in Egypt.**

### **Methods:**

This is a prospective cross sectional observational questionnaire based study. The tested drugs are trastuzumab, lapatinib, sunitinib, everolimus, sorafenib, cetuximab, panitumumab, bevacizumab and erlotinib.

Conceptual development, construction of domains and item pool:

An independent variable, sometimes called an experimental or predictor variable, is a variable that is being manipulated in an experiment in order to observe the effect on a dependent variable, sometimes called an outcome variable.<sup>(6)</sup>

The questionnaire of the current study aims to measure one outcome variable, physician knowledge about pharmaceutical perspectives of cancer drugs. Five predictor variables(domains) were used initially to measure the outcome variable namely, knowledge about toxicity profile, drug-drug interaction, drug-food interaction, methods of preparation for IV drugs, relation to meals for oral drugs. Four items (Questions) were used to ask about the five domains.

The study was designed to be done on two waves; each wave will evaluate 9 drugs. (The current study is the first wave).

The idea of the study is registered on [www.clinicaltrial.gov](http://www.clinicaltrial.gov) NCT02630979.

The study has got the approval from the Institutional Review Board (IRB) of the Clinical Oncology department, Faculty of Medicine, Ain Shams University in October 2015. The questionnaire is a pre-coded, structured, self administered type; it is a closed ended questionnaire.

### **Questionnaire validation:**

Seven experts of professional clinical oncologists were selected as independent committee to re-evaluate the relevance of each question as a tool for measuring the physician's knowledge about pharmaceutical perspectives of cancer drugs. Experts evaluated each question on a 4- point likert scale. (1=not relevant, 2=somewhat relevant, 3=relevant, 4= very relevant).

The content validity of the questionnaire was evaluated through three methods. Firstly, average congruency percentage (ACP): to compute the percentage of questions deemed to be relevant for them as a tool for measurement of the outcome, the value has to be >90 for questionnaire validation. Secondly, content validity index for individual items (I-CVI). The panel were asked to review the relevance of each question on a 4-point likert scale (1=not relevant, 2=somewhat relevant, 3=relevant, 4= very relevant). Then for each question number of experts giving 3 or 4 score were counted and divided on seven (total number of experts). For the question to be valid the I-CVI should not be less than 0.78.

Thirdly, S-CVI/Ave: For each question, The number of experts who rated 3or 4 on likert's scale are added and the result is divided on 7 (number of experts). Then the resultant figures are added and divided by the number of questions. For the questionnaire to be valid the mean expert proportion should not be less than 0.90.<sup>(7)</sup>

After this step, Flesch Reading Ease formulas were applied on the questionnaire format to assess readability.<sup>(8, 9)</sup>

The authors of the study propagated the questionnaire through two different methods. The first method was electronic propagation through <https://www.surveymonkey.com/r/Cureandmore>. This web link was sent to the target oncology physicians in Egypt through mail, SMS or cell phone or whats-up application messages, this enabled the research team to expand the sample size and to cover wide geographical areas in Egypt sometimes difficult to reach.

The second method was through hand to hand propagation of a hard copy.

#### **Data extraction:**

Due to nonuniformity of the answer templates from one question to another, the authors of the study in cooperation with the seven experts have selected the particular answer (Don't know) for each question as a tool for measuring the degree of physician knowledge about pharmaceutical perspectives. Expected prescription error score for each drug will be designed accordingly. A template model answer spread sheet was constructed for collecting the frequency of (don't know) for each question.

The frequency of (don't knows) for each question throughout the 9 evaluated drugs will be collected from the questionnaire samples. The 9 drugs will be ranked accordingly in descending order according to the relative frequency of the (don't know) answers.

Rank 1 will acquire score 9 while rank 9 will acquire score 1. Each drug will have X number of different ranks (Where X=number of validated questions) and a corresponding X number of scores. The sum of the acquired scores for each drug will range from 1multiplied by X to 9 multiplied by X.

#### **Designing Expected Prescription Error Score (EPE) score:**

Drugs are categorized as low, intermediate and high EPE score by dividing the range of (1multiplied by X to 9 multiplied by X.) into three equal ranges.

#### **Reliability measurement:**

It is the ability of the instrument to create reproducible results. Each time it is applied on the same persons, similar scores should be obtained. The test retest method is used. The questionnaire is administered another time after three months to a predefined 21 respondents to detect if similar scores are obtained. The initial and repeated scores are calculated and compared by using correlation coefficient formula (Pearson formula).

The correlation coefficient formula measures the degree of relationship between two sets of scores. +/-0.7 to 1 = strong relationship. +/- 0.3 to 0.69= Moderate relationship and +/- 0.0 to 0.29=No to weak relationship.<sup>(10)</sup>

The questionnaire format is anonymous except for the 21 predefined respondents upon whom the test retest was applied.

The following terms and conditions were written on the front page:

1-This questionnaire is a part of a research work.

<https://clinicaltrials.gov/ct2/show/NCT02630979>

2-By answering this questionnaire you are voluntary accepting that your answers will be used in the research NCT02630979.3-The credibility of the answers in this questionnaire is your total responsibility.

#### **Results:**

The four questions were validated (Table1).

ACP and S-CVI/AV were 92.8% and 0.92% respectively indicating validity of the questionnaire (Table 2).

Flesch Reading Ease formulas were applied on the questionnaire format to assess readability; this was done through an online calculator [www.readabilityformulas.com/freetest/six-readability-formula.php](http://www.readabilityformulas.com/freetest/six-readability-formula.php)

The score was 73.4. According to the rules of the Flesch Reading Ease score, a score between 60-70 is largely acceptable.<sup>(8, 9)</sup>

The authors of the study collected 84 answered questionnaires. The scientific degrees of the respondents were: 31% Master degree, 33% were Medical Doctoral degree and 36% were PhDs.

The institutional affiliations of the respondents were: 80% university staff, 3% General Organization of Teaching Hospitals, 8% were Ministry of Health cancer centers, 6% were private oncology centers and 3% were affiliated to Military and Security forces hospitals. 52% of respondents had private clinics while 48% did not.

Each drug acquired 4 scores along the 4 validated questions; the sum of the 4 scores for each drug was calculated to define its EPE score, the 9 evaluated drugs were arranged in descending order accordingly.

Expected prescription error score will range from 4 to 36. Low, intermediate and high scores are 4-14, 15-25, 26-36 respectively (Table 3).

Erlotinib and trastuzumab are the drugs with the highest and lowest EPE scores respectively.

A high correlation coefficient value was detected between the initial and repeated answers of the respondents. Pearson's coefficient=1.00 indicating reliability of the questionnaire (Table 4).

## **Discussion:**

Questionnaires are the most frequently used data collection method in educational and evaluation research. Questionnaires help to gather information on knowledge, attitudes, opinions, behaviors, facts, and other information.<sup>(11)</sup> Egypt is one of the major countries in North Africa consuming chemotherapy drugs. Up till now there is no data collection for the prescription errors of these drugs.

Validity of a questionnaire based survey is the degree to which the assessment measures what it is supposed to measure. Valid questionnaire helps to collect better quality data with high comparability which reduces the effort and increase the creditability of data.<sup>(12)</sup>

Average congruency percentage test is a well known tool for assessing the content validity of a questionnaire and is attributed to Popham<sup>(13)</sup>. Waltz and his colleagues advised that an ACP of 90% or higher would be considered acceptable.<sup>(14)</sup>

Average congruency percentage test, content validity index test for individual items and for scale were used for assessing the content validity of this study questionnaire. The results revealed that the ACP =92.8% and the S-CVI/AV=0.92% and this confirms the validity of the content of the current questionnaire form.

One of the most important items in evaluating a questionnaire is the readability test. In the Flesch reading-ease test as one of the most popular tests applied to evaluate questionnaire modules, higher scores indicate material that is easier to read; lower numbers mark passages that are more difficult to read.<sup>(14)</sup> The U.S. Department of Defense uses the reading ease test as the standard test of readability for its documents and forms. Florida requires that life insurance policies have a Flesch reading ease score of 45 or greater.<sup>(15)</sup>

After designing the questionnaire of the current study, Flesch reading ease score was applied through an online calculator. Our text scale measured 73.4 indicating that the module is fairly easy to read. The field pilot test for any questionnaire needed 50 to 100 respondents for proper data collection.

In the current study, 84 samples were collected in the field pilot. Hence, the sample size can be considered adequate for proper data generation.

Descriptive statistics is usually used for data analysis of a questionnaire. The statistical distribution of the item scores are revised, any redundant items should be excluded, each question should elicit a normally distributed set of responses across subjects, there should be no skew. SPSS output can be used to look for skewness and standard error skew. For each item (Question) the skewness is divided by its standard error to

form a Z score, if the result is greater than 1.96 then the skewness is significant and the item should be eliminated.<sup>(16)</sup>

In order to apply descriptive statistics on the resultant data from the questionnaire, the answers of the respondents should be on a 4 or 5 points Likert's scale template.

The answers of the questionnaire of the current study differ from one question (Item) to another and it is not on a Likert's scale template. Hence, the data extraction by tracking the statistical distribution of the item scores can't be applied on the current study.

The authors of the study implemented a new method for data extraction upon which the EPE score was designed. The authors defined the particular answer (Don't know) as the answer denoting a defect in the knowledge of the treating physicians with some crucial pharmaceutical perspective of the prescribed drugs. The relative frequency of the unknowns in the answers of each question along the 9 evaluated drugs was collected. Within each question, the drugs were ranked in ascending order from 1 to 9 (Highest to lowest frequency of don't knows respectively). Furthermore, a reversed scores will be assigned for the ranks such that rank 1 will acquire score 9 while rank 9 will acquire score 1. Each drug will have 4 different scores (for the 4 questions) and their sum will range from 4 to 36. Drugs will be arranged in descending order according to the acquired scores. Drugs with higher scores are supposed to have high expected EPE score and should be scheduled for teaching tutorials for the treating physicians to improve the quality of cancer care in Egypt. Test-retest reliability is the degree to which scores are consistent over time. It indicates score variation that occurs from testing session to testing session as a result of errors of measurement. Problems: Memory, Maturation, Learning.<sup>(17)</sup>

The questionnaire of the current study was applied on predefined respondents in two different settings three months apart. Pearson's coefficient was used to test the reliability through detecting the degree of correlation between the answers in both settings. Pearson's coefficient =1.00 indicating high correlation and high reliability of the questionnaire.

## **Conclusion:**

The questionnaire based EPE score can be considered as a flexible, valid and reliable tool for measuring the degree of orientation of clinical and medical oncologists with the pharmaceutical perspectives of expensive cancer drugs in Egypt.

The drugs were arranged in descending order for the priority of subjection to national teaching tutorials for enhancing the quality of cancer service in Egypt. Erlotinib is the drug with the highest EPE score while trastuzumab is the drug with the lowest EPE score.

**Acknowledgment:** The authors acknowledge all oncology colleagues who enriched this study with their valuable answers for the study questionnaire.

**FUNDING:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Disclosures:** The authors have declared no conflict of interest.

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