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The prevalence of major drug-drug interactions in older adults with cancer and the role of clinical decision support software

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ABSTRACT

Objectives: Drug-drug interactions (DDIs) represent an escalating concern for older adults attributed to polypharmacy, multi-morbidity and organ dysfunction. Few studies have evaluated the prevalence of major DDIs and the variability between DDI detection software which confuses management.
Materials and Methods: Prevalence of major DDIs was examined as a secondary analysis of outpatients aged ≥65 years. Demographic and clinical information was collected from electronic health records including age, sex, race, cancer type, comorbidities, and medications. All DDIs were screened by a clinical pharmacist using Lexi-Interact® and Micromedex®. Major DDIs were defined as Lexi-Interact® category D or X and/or Micromedex® category major or contraindication. Summary statistics of patient characteristics and DDIs were computed.
Results: Our cohort included 142 patients (mean age, 77.7 years; 56% women, 73% Caucasian). The mean medications was 9.8 including 6.7 prescriptions, 2.6 non-prescriptions, and 0.5 herbals. Lexi-Interact® identified 310 major DDIs in 69% of patients (n = 98) with an average of 2.2 DDIs per patient. Micromedex® identified 315 major DDIs in 61% of patients (n = 87) with an average of 2.2 DDIs per patient. DDIs mostly involved opioids, antiplatelets, electrolyte supplements, antiemetics, and antidepressants. Variability existed with the severity rating reporting of the clinical decision support software.
Conclusions: There was a high prevalence of major DDIs in older adults with cancer. Utilizing clinical decision support software was beneficial for detecting DDIs however, variability existed with severity reporting. Future studies need to identify the relevant DDIs with clinical implications in order to optimize medication safety in this population.

1. Introduction

Drug-drug interactions (DDIs) represent a mounting public health concern involving the medical management of older adults. Drug-drug interactions are of concern because these interactions can lead to adverse drug events in which the intended therapeutic effect or safety of a medication is altered by the administration of another substance (e.g., drug, herb, food, formulation excipient/container) [1]. Older adults are inherently predisposed to an increased risk for DDIs attributed to disease and aging physiology (e.g., alterations in pharmacodynamics and pharmacokinetics) [2–4]. Other possible drivers that predispose older adults to an increased risk for DDIs is the high prevalence of polypharmacy (e.g., concurrent use of five or more medications including prescription, over-the-counter and herbal supplements), multi-morbidity, fragmented coordination of care among healthcare providers, national guideline recommendations for managing certain disease states, provider prescribing cascades (a medication is mistaken and/or interpreted as a new medical symptom and subsequently, a new medication is prescribed for treatment in a cyclical manner), and communication failures between patients and providers [5–8]. Even though the use of many medications may be favorable for the management of specific medical conditions, the increased risk for DDIs can be an unintended consequence that can lead to morbidity, treatment failures, and increased healthcare utilization [1,3]. For older adults with cancer, DDIs can involve anticancer therapies, supportive care medications (e.g., pain, nausea/vomiting), prescription medications for chronic diseases, non-prescription/over-the-counter medications and herbal supplements. Information on drug-herb interactions remains limited because many patients may omit that they are taking herbal supplements due to lack of direct inquiry, anticipation of provider disapproval, or because of the perception that disclosure is irrelevant to their conventional cancer

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management because of beliefs that such medications are safe and non-toxic (compared to conventional drug therapies) [9,10]. In specific cohorts of older adults with cancer, the reported prevalence of DDIs ranged from 2% to 77%, respectively [11–24]. Such wide-ranging variability is likely credited to the inconsistent study designs and methodologies used for screening/assessing potential DDIs (e.g., medication review by a pharmacist, clinical decision support software), many studies were limited to a single institution cohort or had wide-spread heterogeneity involving patient populations. Additionally, there were inconsistencies regarding definitions for DDIs (e.g. minor-, moderate-, major-, severe-interactions) and determining what DDIs were clinically significant based on the strength and reliability of scientific sources recognizing that most information is based on in-vitro studies. The National Comprehensive Cancer Network (NCCN) Older Adult Oncology Guidelines recommend a thorough evaluation to identify and manage medication related problems which includes assessing for DDIs [25]. The NCCN guidelines do not provide specific guidance on which providers (e.g., oncologists, nurses, pharmacists, medical assistants) should be performing screening assessments for potential DDIs nor the optimal approach for DDI screening assessment (e.g., comprehensive medication review by a clinical pharmacist, consultation with a clinical pharmacologist, utilization of clinical decision support software). Additionally, the guidelines do not discuss how to manage DDIs once encountered nor do the guidelines identify a unique list of DDIs that are clinically significant and most relevant to older adults with cancer. All of these unanswered questions create the need for increased awareness and education among the oncology healthcare team because of the potential for DDIs to compromise cancer management plans (e.g., morbidity, treatment delays and/or treatment discontinuation) and patient-related health outcomes among older adults with cancer. Based on this, we designed this study to examine the prevalence of major DDIs and to determine concordance among 2 clinical support software systems in a cohort of ambulatory older adults with cancer at our institution.

2. Design and Methods

Our research study was approved by the institutional review board at our institution. The prevalence of major DDIs was examined as a

Table 1
Classification of potential drug-drug interactions based on clinical decision support software [27,28].

Classification	Description	Classification	Description
Risk rating Lexi-Interact®		Risk rating Micromedex®	
A	No known interaction; data have not demonstrated either pharmacodynamic or pharmacokinetic interactions between the specified agents	Unknown	No known interaction; data demonstrate that the specified agents do not interact
B	No action needed; data demonstrate that the specified agents may interact with each other but there is little to no evidence of clinical concern resulting from concomitant use	Minor	Unlikely need for therapy modification
C	Monitor therapy; data demonstrate that the specified agents may interact with each other in a clinically significant manner. The benefits of concomitant use of these two medications often outweigh the risks. An appropriate monitoring plan should be implemented to identify potential negative effects. Dosage adjustments of one or more agents may be needed in some patients	Moderate	Possible exacerbation; may require therapy modification
D	Consider therapy modification; data demonstrate that the specified agents may interact with each other in a clinically significant manner. A patient-specific assessment must be conducted to determine whether the benefits of concomitant therapy outweigh the risks. Specific actions must be taken in order to realize the benefits and/or minimize the risks resulting from concomitant use of the agents. These actions may include aggressive monitoring, empiric dosage changes, and/or choosing alternative agents	Major	Potentially life-threatening; consider therapy modification
X	Avoid combination; data demonstrate that the specified agents may interact with each other in a clinically significant manner. The risks associated with concomitant use of these agents usually outweigh the benefits. Concurrent use of these agents should generally be avoided	Contraindicated	Avoid combination
Reliability rating Lexi-Interact®		Reliability rating Micromedex®	
Excellent	Documented in multiple well-controlled investigations (e.g., randomized controlled trials [RCT]). Contradictory evidence is anecdotal or nonexistent	Excellent	Interaction identified based on controlled studies that have clearly established the existence of the interaction
Good	Documented in at least one well-controlled investigation (e.g., RCT) or a plausible interaction with significant supporting evidence from non-RCTs. Evidence of an interaction greatly outweighs evidence of no interaction	Good	Documentation strongly suggests the interaction exists, but well-controlled studies are lacking
Fair	Plausible interaction based on the known pharmacology of the agents which meets one or more of the following criteria: 1) Not formally studied but reported in one or more case studies/series, retrospective reviews, pilot investigations with low sample size or control of extraneous variables, safety monitoring data, drug labeling, or other similar scientifically non-definitive sources; 2) Studied and/or documented but only described in drug labeling; 3) Plausible interaction where studies or cases have yielded inconsistent results; 4) Predicted interaction based on known pharmacodynamic/pharmacokinetic properties and/or animal/in-vitro data	Fair	Documentation is poor but pharmacologic considerations lead clinicians to suspect the interaction exists; or, documentation is good for a pharmacologically similar drug
Poor	Potential interaction meets one or more of the following criteria: 1) A single case report with questionable mechanistic base; 2) Theoretical without sound mechanistic or clinical support; 3) Evidence of no interaction greatly outweighs evidence supporting an interaction	Unknown	Unknown

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