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Reducing Adverse Drug Events:

The Need to Rethink Outpatient Prescribing

Chad Kessler, MD, MHPE, **Michael J. Ward, MD, PhD, MBA**, and **Candace D. McNaughton, MD, PhD, MPH**

Durham VA Medical Center, Durham, North Carolina (Kessler); Vanderbilt University Medical Center, Nashville, Tennessee (Ward, McNaughton)

Gains in life expectancy in the United States are being eroded at least in part due to the use and misuse of prescribed medications.[1] Earlier this year, the US Centers for Disease Control and Prevention reported that life expectancy for some groups in the United States continues to stagnate. Among middle-aged white women, life expectancy decreased, in large part due to medication overdose, opioid use, and liver disease.[2]

In this issue of *JAMA*, the report by Shehab and colleagues[3] suggests that the burden and patterns of adverse health outcomes due to prescribed medications are broader than previously thought. The authors examined data from visits to 58 emergency departments (EDs) included in the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project and identified 42 585 cases of adverse drug events (ADEs) in 2013–2014. The authors estimated that there were 4 ED visits per 1000 individuals for ADEs annually in the United States, and that 27.3% of ED visits for ADEs resulted in hospitalization. Persons aged 65 years or older accounted for an estimated 34.5% of ED visits for ADEs and experienced the highest hospitalization rates (43.6%).

Among adults, the majority of ED visits for ADEs was attributed to anticoagulants, antibiotics, medications for diabetes, and opioids. Among children, antibiotics and neuropsychiatric agents were among the most common causes of ED visits for ADEs. Even though this study specifically excluded ED visits for drug withdrawal, therapeutic failure, occupational exposure, intentional overdose, and recreational drug use, Shehab et al[3] still found an estimated 1.3 million ED visits for ADEs, nearly a 10% increase from 2005–2006. The study was designed to identify ED visits related to ADEs; coders were trained to transcribe rather than interpret clinical notes. The ADEs summarized in this study appear to only be a fraction of the total ADEs in the United States.

Corresponding Author: Chad Kessler, MD, MHPE, Durham VA Medical Center, 508 Fulton St, Durham, NC 27705 (chad.kessler@va.gov).

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Emergency departments within Veterans Health Administration (VHA) medical centers and other integrated health care systems, such as Kaiser Permanente, were not eligible for inclusion in the NEISS-CADES survey and were therefore not included in the study by Shehab et al.[3] The types of excluded institutions are noteworthy because EDs from integrated health systems such as VHA medical centers may provide unique opportunities to address ADEs. More than 2.3 million ED visits occurred across EDs within VHA medical centers in 2013,[4] many of which were for patients older than 65 years, who were prescribed multiple medications, or both. The VHA medical centers and other integrated health care systems that share clinical data across inpatient and outpatient clinical settings may provide an ideal setting to study patients with ADEs in greater detail and develop interventions to prevent, identify, and address ADEs.

According to Rydon-Grange, "When everyone is responsible, no one is responsible."[5] Patients often receive prescriptions from multiple clinicians; for example, the hepatologist manages medications for cirrhosis, the cardiologist manages medications for blood pressure, the orthopedist manages short-term pain medications, the primary care physician or chronic pain specialist manages chronic pain medications, and the psychiatrist manages medications for depression. In this fragmented health care system, clinicians often hesitate to discontinue medications because of lack of familiarity with the medication or patient. Even when clinicians are familiar with patients, it is difficult to coordinate medications for multiple comorbid conditions (eg, managing diuresis in patients with heart failure and chronic kidney disease).

In acute settings such as the ED, concerns about ADEs due to prescribed medications are often not fully addressed because of the limited scope and time with patients and barriers to communication between physicians in the ED and a patient's primary care team. Within large, integrated health care systems such as the VHA(which has a single, nationwide medical record), communication between ED physicians and other clinicians is more feasible, which enhances the role that the ED can play in providing care for patients. Whether this translates into better health outcomes for patients in integrated systems is unknown but should be carefully studied. Changes are needed across the US health care system to assign the role of primary responsibility to a single clinician or a core group for each patient and ensure the means for easily and effectively communicating what should be a deliberate process of starting, monitoring, and discontinuing prescribed medications across multiple clinicians, caregivers, and health care settings.

Shehab et al[3] describe the reality and daunting challenges that face more than half of patients in the United States who are prescribed chronic medications when they state, "[p]atients in ambulatory care and some postacute care settings can have complex medication regimens, at times prescribed by multiple clinicians, with far less monitoring compared with hospitalized patients." More than 10% of individuals in the United States are prescribed 5 or more medications,[6] which perhaps not coincidentally is approximately the same proportion of those who seek care in the ED annually.[7] It is virtually impossible to take 5 medications exactly as directed,[8] and only an estimated 50% of patients take their medications as prescribed, regardless of the number of prescribed medications. [9,10] Given the risks of drug and diet interactions as well as individual differences in drug metabolism,

physicians should expect and be mindful that patients will likely experience ADEs from at least 1 of their prescribed medications. Therefore, clinicians should focus their efforts on identifying and addressing ADEs when they do occur.

Preventing, identifying, and addressing ADEs from prescribed medications will require systematic rethinking and redesign of how medications are prescribed, monitored, and discontinued, particularly medications for chronic conditions. Clinicians across the continuum of care must be involved in this redesign. Patients with ADEs often seek care in the ED, but these visits are frequently isolated from the rest of the patient's clinical care. The most effective interventions for preventing ADEs will require greater involvement and integration of pharmacists, meaningful implementation and use of medication reconciliation, and the inclusion of patients and their caregivers. Overcoming the insidious and pervasive diffusion of responsibility within the current health care system must be a key component in preventing, identifying, and addressing ADEs from prescribed medications.

The ED and its staff can have an important role in the identification, management, and prevention of ADEs through close collaboration with colleagues in primary care, specialty care, and in the pharmacy. More than 136 million ED visits occur annually in the United States,[11] and the majority of hospitalized patients arrive via the ED.[12] Patients who seek care in the ED are often at important health junctures; they are simultaneously at risk for great harm, but also may have the opportunity to gain considerable benefit from medical interventions. Although the ED plays a critical role in acutely starting, changing, and stopping medications, the medication reconciliation process in the ED is fraught with risk and error due to a combination of patient factors (eg, acute illness, cognitive impairment, anxiety, numeracy and health literacy skills) and system factors (eg, rapid pace of care with competing resource allocation, lack of existing patient-physician relationship).[13]

Medication changes in the ED typically occur during brief discussions with anxious and sometimes acutely ill patients and generally without input or records from the patient's primary care or specialty care clinicians. To accomplish proper and safe medication reconciliation, clinicians need an accurate record of prescribed medications, clear communication with patients about the benefits and risks of prescribed medications, explicitly defined methods for reevaluating their need, and means for communicating with the patient's primary care or specialty care team, all of which are extremely challenging to complete in a rigorous manner during a brief ED visit. Increased integration and use of ED-based pharmacists is a potential solution that may meet many of these needs and could build on existing team-based, inpatient hospital models.

The question remain show to best leverage the existing system to improve the safety of the process of starting, monitoring, and discontinuing medications. Collaboration is needed among physicians and other health professionals in primary care, specialty care, pharmacy, and emergency medicine to answer these questions in the quest for safer models of patient care. Furthermore, this collaboration across health care locations and the continuum of care will affect how much benefit or harm patients receive from prescribed medications. Integrated health care systems can help lead the way through improved care coordination and transition of care models. The work by Shehab et al[3] shines a spotlight on the problem

of ADEs and highlights the need to address this important clinical issue in a more systematic and organized fashion.

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