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Original article

# Validation of a score to identify inpatients at risk of a drug-related problem during a 4-year period

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ABSTRACT

*Objective:* Drug-related problems (DRP) produce high morbidity and mortality. It is therefore essential to identify patients at higher risk of these events. This study aimed to validate a DRP risk score in a large number of inpatients.

*Material and methods:* Validation of a previously designed score to identify inpatients at risk of experiencing at least one DRP in a tertiary university hospital from 2010 to 2013. DRP were detected by a pharmacy warning system integrated in the electronic medical record. The score included the following variables associated with a higher risk of DRP: prescription of a higher number of drugs, greater comorbidity, advanced age, specific ATC groups and certain major diagnostic categories.

*Results:* The study included a total of 52,987 admissions; of these, at least one DRP occurred in 14.9%. After validation of the score (period range, 2010–2013: 0.746–0.764), the area under the curve (AUC) was 0.751 (95% CI: 0.745–0.756).

*Conclusions:* This value is higher than those reported in other studies describing validation of risk scores. The score showed good capacity to identify those patients at higher risk of DRP in a much larger sample of inpatients than previously described in the literature. This tool allows optimization of drug therapy monitoring in admitted patients.



## 1. Introduction

Drug-related problems (DRP) have been defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" (PCNE, 2017). This is a general term that can encompass distinct terms referring to drug safety such as drug-related events, adverse reactions, and medication errors.

The DRP rates reported in the literature vary widely: figures for DRP as a cause of admission range from 2% to 10.3% (Angamo et al., 2017; Kalisch et al., 2012; Runciman et al., 2003; Singh et al., 2011; Pedrós et al., 2014), while in admitted patients ranges from 27.8% (Urbina et al., 2014) to as high as 81% (Blix et al., 2004), with various intermediate values reported by other studies (33 DRP por 100 pacientes ingresados (Bedouch et al., 2009), 58% (Dequito et al., 2011), 64.7% (Roten et al., 2010), 5.7–6.1% (Krähenbühl-Melcher et al., 2007).

This variability is likely due to the distinct terms used, as well as differences in types of hospital, the study population and age, type of admission and the methods used to identify DRP in published studies.

The use of specific drug groups during admission, such as opioids, diuretics, anticoagulants, antimicrobials and/or drugs of the cardiovascular system in general have frequently been implicated in the development of DRP in admitted patients (Bates et al., 1999; Bedouch et al., 2009; Bedouch et al., 2015; Blix et al., 2004; Davies et al., 2009; Krähenbühl-Melcher et al., 2007; Viktil et al., 2004). This is the result of greater complexity in certain diseases (Franz et al., 2012; Masoudi and Krumholz, 2003; Wong et al., 2011).

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DRP among inpatients have been associated with high morbidity and mortality (Baena et al., 2014; Kongkaew et al., 2008; Nickel et al., 2013; Patel and Zed, 2002; Singh et al., 2011; Zargarzadeh et al., 2007). Thus, the mortality risk has been reported to be 1.88 (95% CI, 1.54–2.22) (Bates et al., 1997) during admission and to increase hospital stay by 1.91–4.6 days, (Bates et al., 1997; Classen et al., 1997) increasing costs by between $2262 and 4685 (Bates et al., 1997; Classen et al., 1997).

Several strategies have been associated with an increase in medication safety, such as the implementation of electronic prescription and some integrated clinical decision support systems. These have been associated with a decrease in the risk of medication errors and adverse drug events (Ammenwerth et al., 2008; Prgomet et al., 2017; Radley et al., 2013; Reckmann et al., 2009; Westbrook et al., 2015), as well as cost reductions (Ahmed et al., 2016; Eslami et al., 2008; Kaushal et al., 2006; Westbrook et al., 2015).

The identification of patients at higher risk of DRP is essential to allow closer monitoring of their drug treatment and to reduce their risk of experiencing a DRP (Davies et al., 2009; Khan, 2013; Parameswaran Nair et al., 2016a, 2016b; Zopf et al., 2008).

The implementation of the Computerized Physician Order Entry (CPOE) in the Hospital del Mar (Barcelona, Spain) was progressive, beginning in 2007. The Pharmacy Service developed in 2009 a score to identify inpatients at risk of a DRP and identified age, polypharmacy, greater severity as measured by the Charlson score, certain Anatomical Therapeutic Chemical (ATC) groups (https://www.whocc.no/atc_ddd_index/, 2017) and some major diagnostic categories as factors increasing the likelihood of a DRP during admission (Urbina et al., 2014).

Given that this score was obtained in a limited cohort of patients, the aim of this study was to test it in a larger cohort over a longer period of time.

## 2. Material and methods

### 2.1. Study design

The present prospective cohort study was performed in patients admitted to a 400-bed university hospital in Barcelona (Spain) during a 4-year period.

This study was approved by an independent ethics committee (Comitè Ètic d'Investigació Clínica del Parc de Salut Mar) (2016/6576/I).

No additional informed consent was required.

### 2.2. Study period

In a previous study, a score was designed, based on patients admitted to Hospital del Mar (Barcelona, Spain) in 2009 (Urbina et al., 2014). In the present study, the score was validated in a broader cohort of patients admitted during a 4-year period (2010–2013).

### 2.3. Setting

Tertiary university hospital with 431 beds (413 conventional beds plus 18 beds for critically-ill patients). The catchment area of the hospital has around 300,000 inhabitants living in two urban districts (http://www.bcn.cat/estadistica/catala/index.htm, 2017). The services provided by the hospital encompass acute medical and surgical care.

### 2.4. Patient population

To validate the score, the same exclusion criteria were adopted as those used to design the score to identify patients at risk of a DRP (Urbina et al., 2014). Thus, we excluded patients admitted directly to the critical care unit and/or those aged 18 years or younger. Likewise, admissions to the emergency department without hospital admission, or admission to the emergency department observation unit or resuscitation unit were also excluded because these units lacked the CPOE system in 2009.

The CPOE can be accessed by health professionals through the computerized medical records system of the hospital. Within the CPOE, there is a pharmacy DRP warning system that can be used by the pharmacy service. Both the CPOE and the DRP warning system have been previously described in detail (Urbina et al., 2014).

### 2.5. Drug-related problem-risk score

The present study used a previously designed score (Urbina et al., 2014). To design the score, data were used from patients admitted between January and August in 2009 to a tertiary university hospital (training set). The variables associated with having at least one DRP were identified by a multivariate binary logistic regression model and were used to compute the DRP risk score. This score was subsequently validated in a group of patients admitted between September and December 2009 (validation set). Currently, work is being carried out with the Informatics Service for its implementation in the CPOE and its use as a tool for the rapid and routine detection of DRP.

In agreement with the design of the score (Urbina et al., 2014), the following variables were significantly associated with the risk of DRP in inpatients: age older than 60 years (OR, 1.197), higher comorbidity (OR, 1.183), a higher number of prescribed drugs (OR, 3.335), diagnoses of some major diagnostic category (MDC) (Averill et al., 2007) and the prescription of drugs from certain ATC groups (Table 1).

### 2.6. Data collection

Admitted patients were classified according to whether they had a DRP or not during admission. DRP were identified by a team of clinical pharmacists through the CPOE.

Causes of DRP were considered according to the classification of the Pharmaceutical Care Network Europe (event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes).

A consensus was reached among clinical pharmacists on the identification of DRP raising the strongest doubts, in order to reduce bias.

**Table 1**
Variables associated with DRP.

| Variable | OR (95% CI) | Points |
|---|---|---|
| Age > 60 years | 1.197 (1.051–1.364) | 1 |
| Charlson index ≥ 2 | 1.332 (1.183–1.499) | 1 |
| Number of drugs during hospitalization > 10 | 3.335 (2.956–3.763) | 3 |
| MDC Others | 1.393 (1.056–1.838) | 1 |
| MDC Nervous system | 1.393 (1.002–1.937) | 1 |
| MDC Circulatory system | 1.892 (1.400–2.557) | 1 |
| MDC Digestive system | 1.393 (1.042–1.863) | 1 |
| MDC Musculoskeletal system and connective tissue | 1.937 (1.432–2.619) | 1 |
| MDC Kidney and urinary tract | 1.616 (1.169–2.235) | 1 |
| ATC C: cardiovascular system | 1.546 (1.352–1.769) | 1 |
| ATC H: hormone therapy | 1.198 (1.050–1.367) | 1 |
| ATC J: systemic, anti-infectious therapy | 1.913 (1.696–2.157) | 1 |
| ATC S: sensory organs | 2.559 (1.717–3.814) | 2 |
| ATC V: various | 2.181 (1.679–2.834) | 2 |

DRP, drug-related problem; MDC major diagnostic category; ATC, Anatomical Therapeutic Chemical classification system; OR, odds ratio.

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