Research, Society and Development, v. 10, n. 7, e9610715759, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i7.15759

Divergences between mHealth drug interaction checkers: a highlight on HIV hospitalized patients therapy

Divergências entre aplicativos de interações medicamentosas mHealth: um enfoque na terapia de pacientes hospitalizados com HIV

Divergencias entre las aplicaciones móviles de interacciones farmacológicas: con énfasis en la terapia de pacientes hospitalizados con VIH

Received: 05/04/2021 | Reviewed: 05/11/2021 | Accept: 06/01/2021 | Published: 06/14/2021

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Abstract
Introduction: Mobile health (mHealth) apps have been involved in contemporary clinical practice in potential drug-drug interactions (pDDIs) research. However, available pDDIs information may differ between apps, which could impact the success of patient's drug therapy. This study analyzed the performance of the mHealth apps in a context of pharmacotherapy prescribed to HIV/AIDS hospitalized patients. Methods: Cross-sectional study was conducted in a referral hospital for infectious diseases, central Brazil. Drug prescriptions were selected randomly by census. A pDDIs prevalence, severity classification as well the agreement of information and performance of different mHealth checkers were analyzed. Free access mHealth apps were selected: Drugs®, EpocratesRx®, and Micromedex® (considered as reference app). Analysis of sensitivity, specificity, positive or negative predictive values (PPV or NPV) was conducted. Results: The majority of 33 HIV/AIDS hospitalized patients was males, young adults, with opportunistic infections despite of a recent HIV diagnosis. 373 drugs were prescribed with 461 pDDIs identified by mHealth checkers. The pDDIs prevalence was 13.9% (12.4-15.6), 22.2% (20.1-24.5) and 24.8% (22.9-26.8) in Micromedex®, EpocratesRx® and Drugs®, respectively. Micromedex® classified most of pDDIs (71.2%) as major, while Drugs® (67.6%) and EpocratesRx® (84.8%) classified most of them as minor. In comparison with Micromedex®, Drugs® or EpocratesRx® showed none (K<0.00) or little (K=0.11) agreement in identification of pDDIs, respectively. Performance analyzes showed that Drugs® presented greater sensitivity (75.4%), however, the results of specificity, PPV, NPV, and accuracy were similar by both apps when compared to the reference. Conclusion: The mHealth drug interaction checkers presented important divergences in the results of identification, classification of severity and prevalence rate of pDDIs.
Keywords: Drug prescriptions; Mobile device; HIV Infections; Drug interaction; Mobile health; Smartphone.

Resumo
Introdução: Os aplicativos móveis em saúde (mHealth) desempenham importante papel na investigação de interações medicamentosas potenciais (IMP). No entanto, as informações de IMP por eles apresentadas podem diferir entre si, e afetar a terapia medicamentosa do paciente. Este estudo analisou o desempenho de aplicativos mHealth em um contexto de pacientes vivendo com HIV/AIDS hospitalizados. Métodos: Foi realizado estudo transversal em um hospital de referência em doenças infecciosas da região centro-oeste do Brasil. As prescrições de medicamentos foram

selecionadas aleatoriamente por censo. A prevalência de IMP, a classificação de gravidade, bem como a concordância de informações e desempenho de diferentes aplicativos móveis foram analisados. Foram selecionados os aplicativos mHealth de acesso gratuito: Drugs®, EpocratesRx® e Micromedex® (considerado como aplicativo de referência). Foi realizada análise de sensibilidade, especificidade, valores preditivos positivos ou negativos (VPP ou VPN). Resultados: A maioria dos 33 pacientes hospitalizados com HIV/AIDS eram do sexo masculino, adultos jovens, com infecções oportunistas, apesar de um diagnóstico recente de HIV. 373 medicamentos foram prescritos, com 461 IMP identificados pelos aplicativos mHealth. A prevalência de IMP foi de 13,9% (12,4-15,6), 22,2% (20,1-24,5) e 24,8% (22,9-26,8) no Micromedex®, EpocratesRx® e Drugs®, respectivamente. Micromedex® classificou a maioria das IMP (71,2%) como maiores, enquanto Drugs® (67,6%) e EpocratesRx® (84,8%) classificaram a maioria delas como menores. Em comparação com Micromedex®, Drugs® ou EpocratesRx® mostraram nenhuma (K<0,00) ou pouca (K=0,11) concordância na identificação de IMP, respectivamente. As análises de desempenho mostraram que Drugs® apresentou maior sensibilidade (75,4%), porém, os resultados de especificidade, VPP, VPN e acurácia foram semelhantes nos dois aplicativos quando comparados à referência. Conclusão: Os aplicativos mHealth apresentaram divergências importantes nos resultados da identificação, classificação de gravidade e taxa de prevalência de IMP.
Palavras-chave: Prescrições de medicamentos; Dispositivo móvel; Infecções por HIV; Interação medicamentosa; Saúde móvel; Smartphone.

Resumen

Introducción: Las aplicaciones móviles en salud (mHealth) se han involucrado en la práctica clínica contemporánea en la investigación de interacciones farmacológicas potenciales (IFP). Sin embargo, la información de IFP disponible puede diferir entre aplicaciones, lo que podría afectar el éxito de la farmacoterapia del paciente. Este estudio analizó el rendimiento de las aplicaciones mHealth en un contexto de farmacoterapia prescrita a pacientes hospitalizados por VIH/SIDA. Métodos: Estudio transversal realizado en un hospital de referencia por enfermedades infecciosas, centro de Brasil. Las recetas de medicamentos se seleccionaron aleatoriamente mediante censo. Se analizó la prevalencia de IFP, la clasificación de gravedad, así como la concordancia de la información y el desempeño de diferentes verificadores de mHealth. Se seleccionaron aplicaciones de mHealth de acceso gratuito: Drugs®, EpocratesRx® y Micromedex® (considerada como aplicación de referencia). Se realizó análisis de sensibilidad, especificidad, valores predictivos positivos o negativos (VPP e VPN). Resultados: La mayoría de los 33 pacientes hospitalizados por VIH/SIDA eran hombres, adultos jóvenes, con infecciones oportunistas a pesar de un diagnóstico reciente de VIH. Se recetaron 373 medicamentos con 461 IFP identificados por los verificadores de mHealth. La prevalencia de IFP fue 13,9% (12,4-15,6), 22,2% (20,1-24,5) y 24,8% (22,9-26,8) en Micromedex®, EpocratesRx® y Drugs®, respectivamente. Micromedex® clasificó la mayoría de los IFP (71,2%) como mayores, mientras que Drugs® (67,6%) y EpocratesRx® (84,8%) clasificaron a la mayoría de ellos como menores. En comparación con Micromedex®, Drugs® o EpocratesRx® no mostraron ninguna (K<0,00) o poca (K=0,11) concordancia en la identificación de IFP, respectivamente. Los análisis de rendimiento mostraron que Drugs® presentó mayor sensibilidad (75,4%), sin embargo, los resultados de especificidad, VPP, VPN y exactitud fueron similares por ambas aplicaciones en comparación con la referencia. Conclusión: Los verificadores de interacciones medicamentosas de mHealth presentaron importantes divergencias en los resultados de identificación, clasificación de gravedad y tasa de prevalencia de IFP.
Palabras clave: Prescripciones de medicamentos; Aplicaciones móviles; Infecciones por VIH; Interacciones farmacológicas; Telemedicina; Teléfono inteligente.

1. Introduction

Even in the post antiretroviral therapy (ART) era, there is still a high number of hospitalizations of people living with HIV (PLWH) (Crum-Cianflone et al., 2010; Nunes, Caliani, Nunes, Silva, e Mello, 2015). Public Health System data showed more than 25.000 admissions occurred in Brazil in order to treat conditions related to HIV (Brasil, 2019). These individuals are frequently under the risk of potential drug-drug interactions (pDDIs) occurrence due to the concomitant use of different drugs for HIV treatment and associated conditions (Ramos, Japiassú, Bozza, e Guaraldo, 2018; Smith e Flexner, 2017).

In this context, electronic databases, designed to identify pDDIs, are important support tool in health care assistance and contribute to reducing the occurrence of harm to patients related to adverse drug reaction (ADRs) (Cascao, 2017; GV Ramos et al., 2018). Currently**,** mobile health (mHealth) apps have been importantly applicable in contemporary clinical practice (Keney, Achampong, e Attah Snr., 2018; WHO, 2011) and it has been used to search pDDIs, especially in high complexity clinical patients in concurrent treatment with multiple drugs (Ramos et al., 2018; Ramos, Guaraldo, Japiassú, e Bozza, 2015). In line with the third global challenge proposed by the World Health Organization (WHO) these tools have been

contributing to improve access to drug information and support clinical decisions for their safe and rational use (Aungst, Miranda, e Serag-Bolos, 2015; WHO, 2017).

In the literature, there is a lack of mHealth pDDIs information in the context of HIV/AIDS hospitalized patients. Despite the importance of its use, these tools may present differences in available pDDIs information, which could affect the best evidence-based clinical decision by health professionals (Fung, Kapusnik-Uner, Cunningham, Higby-Baker, e Bodenreider, 2017). This study aims to determine the prevalence of pDDIs in HIV/AIDS hospitalized patients identified by mHealth apps. We also intended to classify such interactions according to severity, as well as to evaluate the performance of the mHealth drug interaction checkers.

2. Methodology

Study participants and design

This is a cross-sectional study conducted in a public hospital, medium-sized and high complexity, referral for infectious diseases in central Brazil, 2018. This study was approved by the Research Ethics Committee of State Hospital for Tropical Diseases Dr. Anuar Auad under registration CAAE. 81074117.8.0000.0034. Since this is a study that evaluated secondary data from medical records, consent form was not required. To guarantee the confidentiality of the information and the privacy of the subjects involved in this study, only the researchers had access to the information collected and the access to it was through an alphanumeric password. During the data collection stage, any information that could identify the participating individuals was omitted. Although there is no direct benefit to the patients involved, we believe that this study that compared the information available from these mHealth apps can help healthcare professionals to make the best evidence-based clinical decision in the care of patients in the context of polypharmacy.

A hospital census was carried out on a randomly defined date by means of an electronic draw (www.sorteador.com.br). The daily hospital census is to count and record every hospital day (24 hours), the number of occupied and vacant beds in inpatient units and hospital services (Brasil, 2007). On the date drawn, there were 72 hospitalized patients, of these, those diagnosed with HIV/AIDS (n=33) and their prescriptions were selected. Data collection took place on a single day, in March 2018. Data were collected using a specific form in an electronic medical record. Data on sociodemographic characteristics, clinical-laboratory and pharmacotherapeutic profile of the individuals were accessed.

Results from laboratory tests: (a) viral load quantification and (b) $CD4^+$ T cells count, were obtained from Public Health Data (SISCEL), from the Ministry of Health. Drugs were classified according to their Anatomical Therapeutic Chemical classification by the WHO (WHO, 2018).

mHealth evaluation

The mHealth drug interaction checkers were selected considering its relevance application in scientific studies. We also considered the free access and/or made accessible to Brazilian health professionals and if it were available through the Google Play Store® (Google Inc., CA, USA). The mHealth apps selected were: (a) Drugs.com® Medication Guide, version 2.8.7 (Drugsite Trust, Auckland, NZL), (b) Epocrates Rx®, version 18.6 (Epocrates Inc, CA, USA) and (c) Micromedex® Drug Interactions, version 2.8.0 (Thomson Reuters Healthcare Inc., CO, USA).

Drugs® is a free mobile health app, providing access to personalized health information for healthcare professionals and consumers. The information available comes from the American Society of Health-System Pharmacists (ASHP), Food and Drug Administration (FDA), Truven Health Analytics, Harvard Health and Cerner Multum (Drugs, 2021). Epocrates® is an application that has a free version and a paid version, developed by the company Athenahealth. Its editorial process is carried out by health professionals, who analyze information from the primary literature, recommendations from specialized societies,

clinical guidelines, manufacturer's instructions, standard medical references and FDA drug safety alerts (Epocrates, 2021). Micromedex® is an app accessed through payment, developed by the company Truven Health Analytics. The information provided is developed by an in-house editorial team, clinically trained, with experience in research methodology, and accredited by the National Institute of Excellence in Health and Care (NICE) (IBM, 2018). In Brazil, it is made available free of charge to health professionals linked to the respective professional council, through the Evidence-Based Health Portal, created by the Ministry of Health in partnership with the Coordination of Superior Level Staff Improvement (CAPES/MEC), (Brasil, 2014).

The nomenclature of the active pharmaceutical principle was used to identify pDDIs, which were classified by severity in two groups: major or minor. These groups were created according to similar parameters adopted in previous studies (Cascao, 2017; Kannan et al., 2016) in order to standardize different severity classification presented by the selected mHealth apps: Drugs® (major, moderate, minor), Epocrates Rx® (contraindicated, avoid/use alternative, monitor/modify therapy, caution advised) and Micromedex® (contraindicated, major, moderate, minor) (Table1).

Table 1. Comparison of pDDIs severity classification according to mHealth apps.

Severity classification	**mHealth apps**		
	Drugs®	**Epocrates Rx®**	**Micromedex®**
Major	Major	Contraindicated or Avoid/Use Alternative	Contraindicated or Major
Minor	Moderate or Minor	Monitor/Modify Therapy or Caution Advised	Moderate or Minor

Source: Authors, based on information provided by mHealth apps.

The prevalence of pDDIs was calculated by the ratio between the number of interactions identified by mHealth app and the number of possible combinations calculated by combinatorial analysis, that was performed considering the pairs of drugs prescribed for each individual, excluding those drugs which data were not available in any of the apps selected.

The prevalence of pDDIs stratified by the mHealth app was calculated as described above, considering the interactions and drug combinations identified by Micromedex®, Drugs® or Epocrates Rx®, respectively. The agreement analysis of pDDIs among mHealth apps was performed and Cohen's kappa coefficient was applied. For this analysis, all drug interactions were considered and their repetitions were excluded.

This study considered Micromedex® as the reference mHealth app due to their recognized use in the scientific literature (Muhič, Mrhar, e Brvar, 2017; Roblek, Vaupotic, Mrhar, e Lainscak, 2015). The parameters of performance of Drugs® and Epocrates Rx® apps were accessed by calculation of its sensitivity, specificity, positive or negative predictive values (PPV or NPV) in comparison to the reference app.

Data analysis

Data were inserted into EpiInfo™ v.7.1.5 (CDC, GA, USA) through double entry, by different operators. Descriptive analyses were performed for categorical and continuous variables. Statistical analyses by STATA v.12.0 (Stata Corp, Texas, USA) and OpenEpi® (v.3.01). The Chi-square test was used to evaluate the significance in the prevalence of pDDIs and severity classification among mHealth apps. Value of $p \leq 0.05$ was considered statistically significant.

3. Results

Among 33 HIV/AIDS patients and its drug prescriptions involved in this study, all of them lived at urban areas, the median age was 38 years old (range, 1-65), most of them were male, with low educational level. More than 90% of the individuals were hospitalized at clinical units, three individuals were at the Intensive Care Unit and the median length of stay was 8 days (range, 1-50). (Table 2).

Table 2. Sociodemographic characteristics of HIV/AIDS hospitalized patients at referral hospital for infectious diseases in central Brazil, 2018.

Variables	n=33	%
Age, years (%)		
<20	1	(3.0)
20- 40	19	(57.6)
41- 59	12	(36.4)
≥60	1	(3.0)
Sex		
Male	25	(75.8)
Female	8	(24.2)
Educational level[a], years		
≤8	18	(90.0)
>8	2	(10.0)
Race		
White	3	(9.1)
Mixed/Black	30	(90.9)
Marital status		
Single	26	(78.9)
Married	5	(15.1)
Separated, divorced, or widowed	2	(6.0)
Occupations[b], (%)		
Domestic workers	5	(20.0)
Bricklayers assistant	3	(12.0)
Administrative assistant	3	(12.0)
Cook	3	(12.0)
Others[c]	11	(44.0)

[a]Data were missing for 13 patients [b]Data were missing for eight patients. [c]Others: pensioned, hairdresser, business owner, physiotherapist, driver, cattle farm worker, salesman, and self-employment. Source: Authors.

More than half of the study population had recent HIV diagnosis (≤5 years), approximately 90% presented $CD4^+$ T *cells* count <500 cells/mm^3, 24 individuals had a detectable viral load, and most of the participants presented HIV-associated comorbidities. Only 13 individuals were using ART, among those nine different regimens were prescribed, and dolutegravir was included in 46% (n=6/13) of them. (Table 3).

Table 3. Clinical, laboratory and ART regimen of HIV/AIDS hospitalized patients at referral hospital for infectious diseases in central Brazil, 2018.

Variables	n=33	%
HIV diagnosis, years[a]		
≤ 5	18	(72.0)
6 – 15	5	(20.0)
≥16	2	(8.0)
Comorbidities[b,c]		
Moniliasis	8	(14.5)
Tuberculosis	7	(12.7)
Neurotoxoplasmosis	6	(10.9)
Pneumonia	6	(10.9)
CMV	5	(9.1)
Cryptococcosis	4	(7.3)
Histoplasmosis	3	(5.5)
Others[d]	16	(29.1)
CD4$^+$ T-cell count[e,f], cells/mm^3		
<200	24	(80.0)
200-499	6	(20.0)
Viral load[e,g], copies/ml		
>1000	21	(84.0)
50 – 1000	3	(12.0)
Undetectable	1	(4.0)
ART, r*egimen*s		
2 NRTIs + INSTIs	6	(46.1)
2 NRTIs + PIs/r	3	(23.1)
2 NRTIs + NNRTIs	3	(23.1)
2 NRTIs + INSTIs + PIs/r	1	(7.7)

Abbreviations: CMV: cytomegalovirus; ART: antiretroviral therapy; NRTIs: Nucleoside Reverse Transcriptase Inhibitors; INSTIs: Integrase Inhibitors; PIs/r: Protease Inhibitors/ritonavir; NNRTIs: Non-Nucleosidic Reverse Transcriptase Inhibitors.
[a]Data were missing for eight patients. [b]Total of 55 comorbidities, some individuals present more than one comorbidity. [c]Diagnosis to clarify for three patients. [d]Others: cellulitis, deep vein thrombosis, disseminated intravascular coagulation, herpes, infection with atypical mycobacteria, leishmaniasis, mucormycosis, pansinusopathy, pneumocystosis, syphilis, type 2 leprosy reaction, urinary tract infection. [e]Value referring to the last laboratory test available. [f]Data were missing for three patients. [g]Data were missing for eight patients. Source: Authors.

In this study, a total of 373 drugs were prescribed with a median of 10 (range, 2-25) drugs per prescription, of which: 115 (30.8%) antiinfective for systemic use; 83 (22.3%) alimentary tract and metabolism and 81 (21.7%) nervous system. Overall, 90 active pharmaceutical principles were identified: 10% (n=9/90) have not been available data in any (human albumin, sodium chloride, chlorpheniramine, domperidone, Ringer's lactate solution and glucose) or in all (dipyrone, tenoxicam and bromopride) mHealth drug interaction checkers selected.

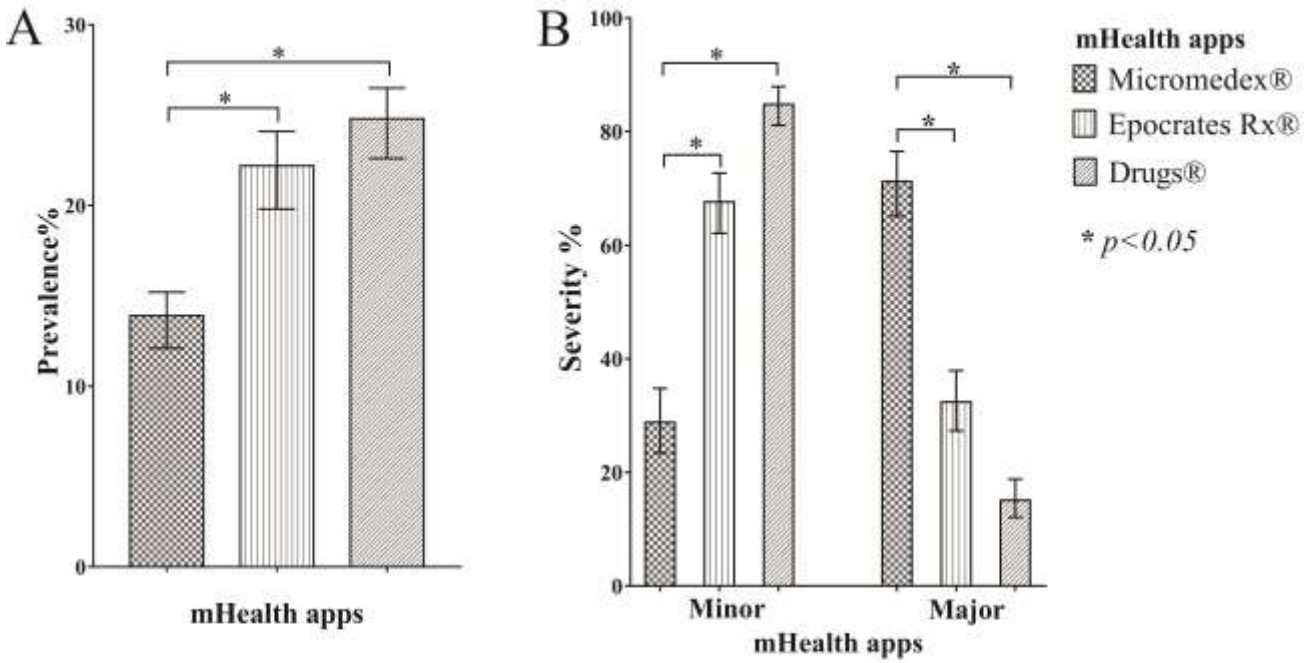
Overall, 84.8% (n=28/33) of drug prescriptions presented at last one interaction. The pDDIs prevalence was 31.5% (CI 95%: 29.4-33.7), considering the ratio between 588 interactions identified by all three mHealth apps and a total of 1.866 drugs combinations, calculated by a combinatorial analysis.

The pDDIs prevalence was highest at Drugs® 24.8% (n=461/1.858) than Epocrates Rx® 22.2% (n=315/1.418) and Micromedex® 13.9% (n=257/1.844) (Figure 1). Additionally, the prevalence ratio analysis showed that drug interactions

identified by Drugs® and Epocrates Rx® were 1.8 and 1.6 times higher than those identified by Micromedex® (p<0.05).

The concordance analysis of drug interactions identification among the reference app, Micromedex® compared to Drugs® or Epocrates Rx® showed none (K<0.00) or little (K=0.11) agreement, respectively. Likewise, the pDDIs severity classification differ significantly (p<0.05) among mHealth apps, while 71.2% (n=183/257) of pDDIs were classified as major by Micromedex®, 67.6% (n=213/315) or 84.8% (n=391/461) were classified as minor by Epocrates Rx® or Drugs®, respectively (Figure 1).

Figure 1. Prevalence and severity classification of pDDIs according to mHealth apps. A, Prevalence of pDDIs by mHealth apps. B, Severity classification of pDDIs by mHealth apps. C, Data of prevalence and severity classification of pDDIs. Error bars: confidence Interval of 95%; The Chi-square used for statistical calculation.



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Potential drug-drug interactions						
mHealth apps	Prevalence		Severity classification			
			Minor		Major	
	%	(CI 95%)	n	(%)	n	(%)
Micromedex®	13.9	(12.4-15.6)	74	(28.8)	183	(71.2)
Epocrates Rx®	22.2	(20.1-24.5)	213	(67.6)	102	(32.4)
Drugs®	24.8	(22.9-26.8)	391	(84.8)	70	(15.2)

Source: Authors.

Potential drug interactions were detected in all 13 prescriptions containing ART. We identified 57 different interactions between antiretrovirals drugs and comedications. Micromedex® identified 28 (49.1%), while Drugs® identified 47 (82.5%) and Epocrates Rx® 34 (59.6%), with statistical significance.

In comparison with Micromedex®, the reference mHealth app, Drugs® presented greater sensitivity in pDDIs identification, however the results of specificity, PPV, NPV and accuracy were similar by both apps. No statistical significance

was observed due to the overlap of the confidence intervals (Table 4).

Table 4. Performance analyses of mHealth apps in the context of pDDIs.

Variables	mHealth apps			
	Drugs®		Epocrates Rx®	
	%	(CI 95%)	%	(CI 95%)
Sensitivity	75.4*	(69.6 - 80.4)	60.9	(54.6 - 66.9)
Specificity	83.0	(81.1- 84.8)	86.3	(84.2 - 88.2)
Positive Predictive Value	41.9	(37.3 - 46.5)	49.5	(43.9 - 55.2)
Negative Predictive Value	95.4	(94.1 - 96.4)	90.9	(89.0 - 92.5)
Accuracy	82.0	(80.1 - 83.7)	81.7	(79.6 - 83.7)

Abbreviations: CI95%: confidence interval of 95%.
*Statistical significance. Source: Authors.

4. Discussion

Overall, the study population consisted of young adults, males, immunosuppressed. All of them had AIDS-associated opportunistic infections. These results corroborate with the clinical and epidemiological profile described in other studies conducted in Brazil and Colombia (Barreneche et al., 2017; Nunes et al., 2015) as well as data from WHO that showed that AIDS-associated infections remain the main cause of hospitalization of PLWH in the world (Ford et al., 2015). A different scenario is observed in developed countries, chronic diseases such as cardiovascular disorders, diabetes, and non-HIV related cancer are the main causes of hospitalization among HIV/AIDS patients (Crum-Cianflone et al., 2010; Kim et al., 2013; Weber et al., 2013).

The drug therapy of HIV/AIDS patients commonly involves polypharmacy practice in order to treat related diseases (Roblek et al., 2015; Smith e Flexner, 2017). A study conducted by Libby et al. (2013), showed a large number of drugs prescribed to HIV/AIDS hospitalized patients our results show agreement in this line. This condition predisposes the occurrence of pDDIs as well as ADRs, which may negatively impact in clinical management, increasing the length of stay and medical costs (Moura, Acurcio, e Belo, 2009; Ramos et al., 2018; Smith e Flexner, 2017).

Many studies have proposed to investigate web database used to search pDDIs among HIV/AIDS context (Marzolini et al., 2011; Ramos et al., 2018; Ramos et al., 2015; Santos, Secoli, e Padoin, 2016). However, the evaluation of these drug interactions through mHealth apps is still an unexplored area, despite the increasing use of these tools in the clinical practice (Keney et al., 2018). Our study presented the results of a pDDIs investigation by three distinct mHealth drug interaction checkers (Drugs®, Epocrates Rx® and Micromedex®) revealing a high prevalence of these interactions and pointed that more than 80% of the prescriptions presented at least one pDDIs

Approximately 40% of participants were using ART, and all prescriptions of these individuals had pDDIs. A study carried out in a university hospital, in the Brazilian capital, showed that among the HIV/AIDS patients using ART 69.4% of the prescriptions presented drug interactions (Nóbrega, 2014). In outpatients, the prevalence of drug interactions appears to be somewhat lower. Studies performed in Brazil and Switzerland showed pDDIs prevalence of 52.2% and 40.0% (Marzolini et al., 2011; Santos et al., 2016). We believe that the high frequency of pDDIs in our study can be attributed to the scenario where the study was conducted, the referral hospital for infectious diseases, that involved patients who had HIV-associated comorbidities, mainly opportunistic diseases.

We observed differences in the identification, classification and prevalence of pDDIs detected by Micromedex®, Drugs® and Epocrates Rx®. In this way our results showed concern about the influence of the database choice to study drug

interactions in a bedside practice. Although this study had focused on the evaluation of mHealth apps, the results described here corroborate studies that investigated pDDIs through different web databases, which also demonstrated relevant variation (Fung et al., 2017; Kannan et al., 2016; G. V. Ramos et al., 2015).

The Micromedex® app, which was chosen as a reference, had the lowest prevalence rate and classified most of the interactions as major severity. In comparison, most of the interactions were classified as minor severity and an increase of approximately 10% in the prevalence rate was shown by the other apps: Drugs® and Epocrates Rx®. These data point to a possible over-identification of pDDIs by Drugs® and Epocrates Rx®, which can cause alert fatigue, when clinicians tend to ignore important alerts (Bryant, Fletcher e Payne, 2014; Roblek et al., 2015).

The performance analysis of mHealth drug interaction checkers demonstrated that Drugs® is the most sensitive. In contrast, both applications presented similar results regarding specificity, positive and negative predictive values as well as accuracy. It should be noted that the low PPV results observed in relation to the reference app revealed low ability to properly identify the pDDIs by these apps in comparison with the reference (Vonbach, Dubied, Krähenbühl, e Beer, 2008).

The present study has great importance in the research line of information on pDDIs made available through mobile health applications, widely used in the contemporary practice of health professionals. The limitations of our study included the subjective choice of Micromedex® as the reference application, the selected restricted population (patients with HIV/AIDS hospitalized), and the lack of information of clinical outcome provided by the pDDIs, which requires a different design study and it wasn't in the scope of this study. We highlighted that our study was conducted in a hospital setting while in the literature, in HIV/AIDS patients context, most of the studies that evaluated pDDIs were conducted in an outpatient setting.

The results presented in this study confirm the necessity to parameterize the information provided by mHealth drug interaction checkers databases, mainly in the identification and classification of pDDIs (Payne et al., 2015; Scheife et al., 2015; Tilson et al., 2016). These procedures could increase the confidence of the information presented by the databases and it will improve clinical practice in a context to reduce patient harm generated by unsafe medication practices (Kongsholm, Nielsen, e Damkier, 2015; Payne et al., 2015; Scheife et al., 2015; Tilson et al., 2016).

5. Conclusion

The present study identified a high prevalence of pDDIs in drug prescriptions of HIV/AIDS hospitalized patients at a referral hospital for infectious diseases in central Brazil. The mHealth drug interaction checkers presented important divergences in the results of identification, classification of severity and prevalence rate of pDDIs. Regarding the reference mHealth in our study, the performance analysis demonstrated greater sensitivity of Drugs®. Similar results of accuracy, specificity, positive and negative predictive value were observed between the databases.

It will be important to develop studies that systematically evaluate the information of pDDIs provided by electronic databases available at literature, as well as the standardization of parameters of identification processes, the classification of interactions among those truly presents clinical relevance.

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