FEDERAL UNIVERSITY OF SERGIPE

CENTER OF BIOLOGICAL AND HEALTH'S SCIENCES

DEPARTAMENT OF PHARMACY

LABORATORY OF FOOD AND BEVERAGE

IRAÊ OLIVEIRA MOURA

IDENTIFICATION OF PHARMACIST'S ROLE FOR PATIENT'S COUNSELING ON FOOD-DRUG INTERACTION - A SYSTEMATIC REVIEW

IDENTIFICAÇÃO DO PAPEL DO FARMACÊUTICO PARA ORIENTAÇÃO DO PACIENTE SOBRE A INTERAÇÃO MEDICAMENTO-ALIMENTO – UMA REVISÃO SISTEMÁTICA

SÃO CRISTÓVÃO, SERGIPE

JANUARY, 2017

IRAÊ OLIVEIRA MOURA

IDENTIFICATION OF PHARMACIST'S ROLE FOR PATIENT'S COUNSELING ON FOOD-DRUG INTERACTION - A SYSTEMATIC REVIEW

AVALIAÇÃO DO CONHECIMENTO E PAPEL DO FARMACÊUTICO PARA ORIENTAÇÃO DO PACIENTE SOBRE A INTERAÇÃO MEDICAMENTO-ALIMENTO – UMA REVISÃO SISTEMÁTICA

Completion of coursework presented as pre-requisite for obtaining a Bachelor's degree in Pharmacy.

Supervisor: PhD Aurélia Santos Faraoni

Co-supervisor: PhD Divaldo Pereira de Lyra Junior

SÃO CRISTÓVÃO, SERGIPE

JANUARY, 2017

SUMMARY

Identification of pharmacist's role for patient's counseling on food-drug interaction - a systematic review

MOURA, I.O[1]; ROCHA, K.S.S[2]; BARROS, I.M.C[3]**;** LYRA JUNIOR[4], D.P; FARAONI, A.S[5*].

[1]Student of Pharmacy. Laboratory of Foods and Beverages (LAAB), Federal University of Sergipe, Brazil. E-mail: irae.moura@yahoo.com.br.

[2]Pharmacist. Laboratory of Teaching and Research in Social Pharmacy (LEPFS), Federal University of Sergipe, Brazil. E-mail: kerilin.farm@gmail.com.

[3]PhD Pharmacist. Laboratory of Teaching and Research in Social Pharmacy (LEPFS), Federal University of Sergipe, Brazil. E-mail: izadoramcb@hotmail.com

[4]PhD Pharmacist and Professor of Pharmacy College of Federal University of Sergipe. Laboratory of Teaching and Research in Social Pharmacy (LEPFS), Federal University of Sergipe, Brazil. E-mail: lyra_jr@hotmail.com.

[5]PhD Pharmacist and Professor of Pharmacy College of Federal University of Sergipe. Laboratory of Foods and Beverages (LAAB), Federal University of Sergipe, Brazil. E-mail: faraoniaurelia@yahoo.com.br.

*Corresponding author: Cidade Universitária "Prof. José Aloísio Campos", Jardim Rosa Elze, São Cristóvão, CEP: 49100-000, Brazil. Tel./fax: +55217931946365.

E-mail: faraoniaurelia@yahoo.com

FINANCIAL SUPPORT:

This study was supported by Fundação de Apoio à Pesquisa e à Inovação Tecnológica de Sergipe (FAPITEC-SE) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (*CAPES*).

ABSTRACT

Introduction: Food-drug interactions represent a growing concern for health services and are clinically significant. There is a lack of published studies in this area. In clinical practice, these interactions can cause problems for the patient, resulting in treatment failure, adverse reactions, and nutritional deficiency. However, the addition of a pharmacist to the multidisciplinary treatment team can improve the identification, prevention, and resolution of problems for the patients that involve drug interactions, as well as, food-drug interactions. **Objective:** To review the literature to identify the role with respect to patients' education about food-drug interactions. **Methods:** The online database search was carried out in the following databases: Pubmed, Scopus, Lilacs, Scielo, and Ebsco in Januaruy, 2017. A new survey was carried out in January 2017 to update the search for articles. The descriptors were "patient education," "knowledge," "patient," "pharmacists," "counseling," "food-drug interaction," and "role," and these words were arranged in different combinations. Then, there were an evaluation of studies, in which the title, abstract, and full text of the studies were eligible. The review was written according to the PRISMA criterion (Preferred Reporting Items for Systematic reviews and Meta-Analyses). **Results:** The search identified 393 related articles, however, only four articles were eligible. The pharmacist's role in the care and guidance of patients is linked to the application of their skills such as optimizing drug therapy, decreasing unwanted adverse effects, therapeutic drug monitoring, adjusting medications based on organ function to the reduction of unfavorable occurrences caused by the interactions between drugs and food. Thus, when the pharmacist is included as an active member of the healthcare team, problems related to food-drug interactions can be reduced and therefore have a large benefit for the patient. **Conclusion:** These studies revealed that the pharmacist has an important role in the detection, prevention, and resolution of problems related to the interaction between drugs and food. The pharmacist also can improve the patient's pharmacotherapy through the development of programs and methods that will help them in clinical practice.

What is already known about this subject:

There are few studies related to this subject, what shows the importance to develop more researches about it. The literature has shown that most articles reviewed involved only interactions between drugs, and failed to include the interactions between drugs and foods that usually occur, provoking unwanted effects such as: potentialization or reduction of the drug's

efficacy.

What this study adds:

In this context of scarcity of published articles related to food-drug interaction, this study becomes relevant to show the importance of pharmacist's expertise, involvement and role in the counseling of patients about food-drug interactions in clinical practice.

INTRODUCTION

According to the WHO, more than 50% of the medicines are prescribed, dispensed, and administered incorrectly around the world.[1]The problems related to medications occur frequently in medical practice and are considered the main causes of health complications and economic and social losses.[2,3,4] Among these problems, highlights the interaction between food and drugs. These interactions can be defined as events when food, or one of its components, interferes with the pharmacokinetic and pharmacodynamic parameters of medicines or when drugs affect the body's nutritional balance.[2]

An interaction is considered to be clinically significant if it alters therapeutic drug response or compromises nutrition status resulting in some degree of malnutrition. The clinical consequences of an interaction are related to alterations in the absorption and effect of the drug or nutrient.[2] This could result in partial or total failure of the pharmacotherapy as well as significant adverse drug reactions (e.g., monoamine oxidase inhibitors increases high levels of tyramine in foods such as cheese, wine, and dairy products).[3] In addition, drugs with a low therapeutic index (lithium, theophylline, and phenytoin) and dosages that require greater control (e.g., anticoagulants) tend to have more clinically significant food-drug interactions.[4]

This type of interaction can be present in different cases and groups of patients. The elderly, obese, critically ill, transplant recipients, patients receiving enteral nutrition, and patients with chronic disease who use multiple medications, for example, can be considered high risk to have some food-drug or drug interactions.[5,6]

According to above findings, the multidisciplinary team should be able to discuss the patients' needs and provide information about their treatment and medicines in order to avoid possible complications and achieve therapeutic success.[7,8] In such a team, the pharmacist should assist to identify medication challenges faced by patients, as well as assisting in preventing of potential issues associated with drug therapy, such as significant drug interactions (including food-drug interactions).[9,10,11]

Although the literature highlights the importance of the multiprofessional team and the pharmacist in the food-drug interaction, there have been few published studies that describe the role of the pharmacist that is linked to ensure the correct use of medications and food, besides counsel patients regarding this interaction. Therefore, the aim of this study was to identify the pharmacist's role in guiding to the patient with respect to food-drug interactions.

METHODS

This systematic review was carried out to identify and evaluate relevant studies' main findings regarding the assessment of the pharmacist's role with respect to patients' education about food-drug interactions. To this end, the following steps were performed:

Identification and selection of studies:

This study was a systematic review of publications from Pubmed, Scopus, Lilacs, Scielo, and Ebsco collected in January 2017. The descriptors used for the search were "patient education," "knowledge," "patient," "pharmacists," "counseling," "food-drug interaction," and "role" which were arranged in different combinations, according each database: "food-drug interaction" AND pharmacists AND "patient education"; "food-drug interaction" AND pharmacists AND knowledge; "food-drug interaction" AND pharmacists AND patient; "food-drug interaction" AND pharmacists AND counseling; "food-drug interaction" AND pharmacists AND role.

Critical appraisal of the studies and data collection:

The following screening process was conducted in three stages. (1) Articles were selected according to the relevance of their titles. (2) Abstracts were evaluated based on the pre-established inclusion criteria: original papers that discussed the interactions between medicines and food, patients' knowledge, and the pharmacist's role in patient education. (3) Articles that met all inclusion criterias were carefully evaluated before initiating the data extraction process.

The excluded studies were those that were either not written in English, Portuguese, or Spanish, had no abstract or details of the methodology used in the research, or were articles that were systematic or literature reviews. Items that appeared in more than one database were considered only once. The analysis of the selected articles was performed by two independent reviewers, with disagreements resolved by consensus, and if necessary a consensus by a third investigator.

The articles selected for the data extraction were examined based on the following variables: (a) geographical location and study setting, (b) type of study, (c) types and number of patients involved in the study, (d) elucidation of the pharmacists' role and pharmaceutical knowledge, (e) tools that assisted in the evaluation of food-drug interactions, (f) interaction between pharmacists and other professionals, (g) drugs involved in the interactions with food, (h) pharmaceutical interventions for food-drug interactions, (i) results of pharmaceutical interventions, and (j) limitations.

Evaluation of the methodological quality of the selected studies:

The methodological quality of the articles was evaluated according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations. [12] Two categories were established in this regard: (1) "yes" when the study met the STROBE criteria and (2) "no" when the STROBE criteria were not met.

This review was written according to the PRISMA statement criterion (*Preferred Reporting Items for Systematic reviews and Meta-Analyses)*, which provides essential information on the methodology and conduction of systematic reviews.[3]

RESULTS

From the five search databases mentioned previously, it was obtained a sample of 393 articles, of which 24 articles were present in more than one database. Therefore, the total number of articles was 369, of which only 78 had relevant titles and were subsequently

submitted for further analysis of their abstracts (Figure 1). It is noteworthy that no relevant studies were found from the Scielo and Lilacs databases.

After reading the abstracts, 29 articles were pre-selected for further evaluation of the full texts. Of these, 25 articles were excluded; 15 articles did not meet the inclusion criteria for the study, seven articles were systematic reviews, one article was a tutorial, one article was written in Japanese, and the full text of one article was not available. At the end of the selection process, only four articles[13,14,15,16] were included in the sample: three were written in English and one in Spanish.

With respect to the location of the studies, two studies were developed in the United States, one in Iran, and one in Argentina. All the studies were developed and carried out in a hospital setting. Thus, the target audience consisted of hospitalized patients, even with certain peculiarities. The number of patients and the type of study conducted were not reported by all the studies in this review. Table 1 describes the general characteristics of the articles that were included in this study.

In the evaluation of specific aspects of the articles (Table 2), the pharmacist's role was found to be associated with clinical practice through assisting in the detection and evaluation of interactions between drugs and food in all the studies in the sample. Another important point showed that the need for the addition of a pharmacist to the multidisciplinary team was mentioned in all the articles in order to improve the clinical condition of patients. Additionally, the limitations of some of the studies are reported in Table 2.

According to the STROBE Statement (Table 3), it could be verified the lack of a more precise and complete description of the studies involved in this review. Half of the studies (50%) did not describe the study design. None of them (0%) defined variables clearly, data source, bias, statistical methods and limitations, as also they did not discuss the generalization (external validity) of the study results.

DISCUSSION

Interactions between drugs and food can influence the success of therapy and treatment.[17,18] This can even cause potential complications for patients, such as toxicity or adverse effects, therapeutic failure, and nutritional deficiency.[18,19] Possibly, patients with

multiple diseases, renal or hepatic failure, patients with autoimmune diseases, newborns, and post-surgery patients are the most susceptible to these food-drug interactions because they make use of polypharmacy.[20] Nowadays, the identification of drug interactions is one of the most relevant issues for pharmacovigilance.[21]

In this review, two of the four studies on the pharmacist's role to instruct the patient about food-drug interactions were carried out in the United States. These results are probably due to the fact that the United States is one of the forerunners in the provision of clinical services associated with the development of new models of pharmaceutical practices.[22,23] On the other hand, in some less developed countries, for a long time the pharmacist was seen solely as a supplier of drugs. However, the reality is changing and improving clinical services is becoming important in patient care. [24,25,26] Therefore, it is necessary that the pharmacist keeps the patient, not the drugs, as the main focus of their professional practice, thereby promoting patient care and providing guidance of medication use.

Although the review only shows articles in a hospital environment, the food-drug interaction can occur at any scope (basic health unit, home ...), [52] and these patients need the guidance of the pharmacist. It is necessary to carry out studies in these other areas to verify the incidence of these interactions and how the pharmacist can avoid them.

The fact that all the analyzed studies have been executed in hospitals, emphasizes the importance of a multidisciplinary team for treatment. According to Samartín et al. 2014, the integration of health professionals in hospitals allows for the combination of complementary skills and the supply of information necessary to achieve the best possible therapeutic results for the patient. Studies show that clinical services provided by pharmacists are important in different environments. In clinics, pharmacists improved the adherence and clinical outcomes in 53.5% of the patients with chronic disease, in contrast to 37.4% of the patients who were not subjected to pharmaceutical monitoring. In hospitals, the correct application of knowledge and practice in clinical pharmacy improved the clinical outcomes of ICU patients and reduced the cost of pharmacotherapy by 35.8%, in a study on anti-infectives and cardiovascular drugs in intensive care units.[27,28,29]

In the multidisciplinary team, when pharmacists work along with doctors, nurses, and nutritionists, they can provide the best treatment for the patient by assessing the most appropriate pharmacotherapy which is both safe and effective, as well as by examining

possible interactions between drug and food. [20,21,30,31] Pharmacists can highlight and identify the needs of differentiated patients that suffer from asthma, chronic obstructive pulmonary disease, osteoporosis, hypertension, diabetes, or those who need enteral nutrition too. [32,33,34,35,36,37,38,39]

Some studies that were reviewed included patients receiving enteral or parenteral nutrition, such as, bariatric patients and premature newborns.[40,41]The type of nutrition that these patients received, given through probes either inserted directly into the stomach or intestine of the patient or intravenously, required special attention for its preparation and administration. [42] In this context, the participation of the pharmacist is important not only for providing counsel to the health team, but also for the detection, prevention, and resolution of problems related to drug-drug interactions and food-drug interactions, envolving dosage form, stability problems, probe problems, necessity of time adjustment.[43,44]

The study by Sánchez et al. (2006) corroborated the results of this study. They reported complications in 78.57% of the patients who used enteral nutrition and medicines concomitantly. [42] Therefore, the addition of a pharmacist to the multidisciplinary team could help indicate potential complications for patients and possible medication errors related to the administration of different drugs and nutrition can be minimized.

All the articles that were analyzed elucidated the role of pharmacists and pharmaceutical knowledge to instruct the patient on the food-drug interaction. In addition, the strategies used to help orient patients to these interactions ranged from leaflets to mentoring programs and became important to monitor the occurrences of interactions, thereby ensuring patients' safety. Studies have shown that the adoption of strategies developed by the pharmacist and/or healthcare team increases the probability of achieving therapeutic success and minimizes the risk of adverse food-drug interactions. [45,46,47,48,49]

In this study, the most professional relationship found was between pharmacists and nurses. Nurses are professionals who have direct patient contact and are therefore, able to overcome any problems related to these food-drug interactions. When nurses associate with the pharmacist, they can assess the problems related to food-drug interactions and help monitor the pharmacotherapy, for example, in establishing the appropriate times for drug administration.[50] In short, we have found that communication and collaboration between the

members of the health care team is necessary to improve the effectiveness of pharmacotherapy with patients and reduce adverse events, as also healthcare costs. [51]

According to the STROBE recommendations, a lack of information regarding sampling may decrease the impact of the review. Therefore, researchers should describe the methods used to establish sample sizes in order to demonstrate increased robustness.[53] Besides, the included articles did not present a totality in any of the recommendations described by Strobe, which shows that the studies in this area did not appear well structured about the subject in question.

This study had some limitations. The age and the clinical condition of the patients in the selected studies were not adequately described. Therefore, the results did not represent a homogeneous sample which consequently, prevented a better analysis of the food-drug interactions. Another limitation was that most articles did not contain a description of the type of studies carried out. In addition, the choice of descriptors may have restricted the results of this study.

CONCLUSION

In this review, it was noted that research on the pharmacist's role to instruct the patient on food-drug interactions was scarce. Moreover, it was observed that when the pharmacist works with other health professionals, they provide better therapeutic results because they reduce the occurrence of adverse food-drug interactions.

In this review, we highlight the scarcity of published articles related to food-drug interactions, which indicates the need for more studies to be conducted in this field, especially in Brazil. Consequently, this review may be of help to researchers who want to understand and investigate this issue, and highlights one of the many important contributions that pharmacists add to clinical practice.

REFERENCES

1. World Health Organization (WHO). The safety of medicines in public health programmes: pharmacovigilance an essential tool. *World Health Organization*. Geneva, 2006.

2. BOULLATA JI, HUDSON LM. Drug-nutrient interactions: a broad view with implications for practice. *J Acad Nutr Diet*. 2012;12(4):506-17.

3. MASON P. Symposium 8: Drugs and nutrition. Important drug–nutrient interactions. *Annual Meeting of the Nutrition Society and BAPEN*, Cardiff International Arena, Cardiff. 2009.

4. MENDES-NETTO RS, SILVA CQV, OLIVEIRA FILHO AD, ROCHA CE, LYRA-JUNIOR DP. Assessment of drug interactions in elderly patients of a family health care unit in Aracaju (Brazil): A pilot study. *African Journal of Pharmacy and Pharmacology*. 2011 Vol. 5(7), pp. 812-818.

5. SALAZAR JA, POON I, NAIR M. Clinical consequences of polypharmacy in elderly: Expect the unexpected, think the unthinkable. *Expert Opin Drug Saf*. 2007;6(6):695-704.

6. JYRKKÅ J, ENLUND H, KORHONEN MJ, SULKAVA R, HARTIKAINEN S. Patterns of drug use and factors associated with polypharmacy and excessive polypharmacy in elderly persons. *Drugs Aging*. 2009;26(6):493-503.

7. CARTER BL, ROGERS M, DALY J, ZHENG S, JAMES PA. The Potency of Team-Based Care Interventions for Hypertension: a meta-analysis. *Arch Intern Med*. 2009 vol 169 (no. 19), oct 26.

8. ARMOR BL, BRITTON ML, DENNIS VC, LETASSY NA. A review of pharmacist contributions to Diabetes Care in the United States. *Journal of Pharmacy Practice*, 2010.

9. OLIVEIRA DR, BRUMMEL AR, MILLER DB. Medication Therapy Management: 10 Years of Experience in a Large Integrated Health Care System. *Journal of Managed Care Pharmacy*, 2010 Vol. 16, No. 3.

10. MAGEDANZ L, SILLIPRANDI EC,SANTOS, RP. Impact of the pharmacist on a multidisciplinary team in an antimicrobial stewardship program: a quasi-experimental study. *International Journal of Clinical Pharmacy*, 2012.

11. HUSSAINY SY, BOX M, SCHOLES S. Piloting the role of a pharmacist in a community palliative care multidisciplinary team: an Australian experience. *BMC Palliative Care*, 2011.

12. SKOUROLIAKOU M., THANOPOULOS MN, MARAVELIAS G, PAPANDREOU P, NTOUNTANIOTIS D et al. Nutrition-drug interactions: A Web-based approach to pharmaceutical care in Greece. *J Am Pharm Assoc (2003).* 2014 Jul 1;54(4):419-26.

13. NAZARI MA, SALAMZADEH J, HAJEBI G, GILBERT B. The Role of Clinical Pharmacists in Educating Nurses to Reduce Drug-Food Interactions (Absorption Phase) in Hospitalized Patients. *Iranian Journal of Pharmaceutical Research* (2011), 10 (1): 173-177.

14. MILLER LG, RAATZ S. Development of a Drug-Food Interaction Discharge Counseling Program. *Nutrition International*. Vol. 3, n. 1, Jan, 1987.

15. CERULLI J, MALONE M. Assessment of Drug-Related Problems in Clinical Nutrition Patients. *Journal of Parenteral and Enteral Nutrition* , vol. 23, n. 4, Jul, 1999.

16. SÁNCHEZ AIG et al. Atención farmacéutica en pacientes con nutrición enteral. *Farm Hosp.* Vol. 30, n. 1, PP. 44-48, 2006.

17. CRUCIOL-SOUZAJM, THOMSON JC. A pharmacoepidemiologic study of drug interactions in a brazilian teaching hospital. *Clinics* (São Paulo). 2006;61(6):515-20.

18. ABBASINAZARI *A M,* SALAMZADEH J, HAJEBI*A*AND G, GILBERT*C B.* The Role of Clinical Pharmacists in Educating Nurses to Reduce Drug-Food Interactions (Absorption Phase) in Hospitalized Patients. *Iranian Journal of Pharmaceutical Research*, 2011:10 (1):173-178.

19. GENSER D. Food and drug interaction: consequences for the nutrition/health status. *Ann Nutr Metab*. 2008:52 Suppl 1:29-32

20. JACOMINI LCL; SILVA NA. Drug interactions: a contribution to the rational use of synthetic and biological immunosuppressants. *Revista Brasileira de Reumatologia*. São Paulo, 2011 Vol. 51, No. 2.

21. CARDOSO MA, AMORIM MAlL. A farmacovigilância e sua importância no monitoramento das reações adversas a medicamentos. *Revista Saúde e Desenvolvimento* 4.2 (2013): 33-56.

22. ANDRADE TU, BARBOSA JLC, LAIGNIER LLM, MATA EF, CASSARO, KOS, et al . Scientific production in pharmaceutical care: comparison between Brazil, USA and Spain. *Braz. J. Pharm. Sci*. 2013, v.49, n.1.

23. BRASIL. Conselho Federal de Farmácia. RESOLUÇÃO Nº 585 DE 29 DE AGOSTO DE 2013.

24. PEREIRA LRL, FREITAS O. The evolution of pharmaceutical care and the prospect for the Brazil. *Brazilian Journal of Pharmaceutical Sciences*, São Paulo, v. 44, n. 4, p. 601-612, 2008.

25. AGUIAR PM,BALISA-ROCHA BJ, BRITO GC, LYRA DP Jr.Pharmaceutical care program for elderly patients with uncontrolled hypertension. *Journal of the American Pharmacists Association: JAPhA*, 2012; v. 52, n. 4, p. 515-518.

26. GUÉRIN A, THIBAULT M, NGUYEN C, LEBEL D, BUSSIÈRES JF. Steps aimed at upgrading a pharmaceutical care sector: The case of surgery, *Ann Pharm Fr*, 2014; 7 2(4):267-86.

27. SPENCE MM, MAKAREM AF, REYES SL, ROSA LL, NGUYEN C, et al. Evaluation of an Outpatient Pharmacy Clinical Services Program on Adherence and Clinical Outcomes Among Patients with Diabetes and/or Coronary Artery Disease. *J Manag Care Pharm.* 2014 Oct;20(10):1036-45

28. ALJBOURI TM, ALKHAWALDEH MS, ABU-RUMMAN AE, HASAN TA, KHATTAR HM, et al. Impact of clinical pharmacist on cost of drug therapy in the ICU. *Saudi Pharm J.* 2013 Oct; 21(4):371-4.

29. MACLAREN R, BRETT MCQUEEN R, CAMPBELL J.Clinical and financial impact of pharmacy services in the intensive care unit: pharmacist and prescriber perceptions. *Pharmacotherapy*. 2013 Apr;33(4):401-10.

30. YAHEYA M, ISMAIL M. Drug-food interactions and role of pharmacist (Review). *Asian Journal of Pharmaceutical and Clinical Research*. Oman. Volume 2, Issue 4, October 2009, Pages 1-10.

31. VERVACKE AL, LORENT S, MOTTE S. Improved venous thromboembolism prophylaxis by pharmacist-driven interventions in acutely ill medical patients in Belgium. *Int J Clin Pharm*. 2014.

32. HEPLER CD, STRAND LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm*. 1990;47(3):533–43.

33. SANTOS PM, NOBLAT L, CRUZ ÁA.A policy of free access to asthma medicines in Brazil: an opportunity for pharmacists to optimize asthma treatment. *Int J Clin Pharm*. 2013;35:510–512.

34. WEI L, YANG X, LI J, LIU L, LUO H, et el. Effect of pharmaceutical care on medication adherence and hospital admission in patients with chronicobstructive pulmonary disease (COPD): a randomized controlled study. *J Thorac Dis.* 2014;Jun;6(6):656-62.

35. DUQUET N. Osteoporosis: treatment and pharmaceutical care**.** *J Pharm Belg.* 2014;Jun;(2):14-24.

36. HIRSCH JD, STEERS N, ADLER DS, KUO GM, MORELLO CM, et al. Primary Care-based, Pharmacist-physician Collaborative Medication-therapy Management of Hypertension: A Randomized, Pragmatic Trial. *Clin Ther.* 2014; Sep 1;36(9):1244-54.

37. WAL P, WAL A, BHANDARI A, PANDEY U, RAI AK. Pharmacist involvement in the patient care improves outcome in hypertension patients. *J Res Pharm Pract.* 2013;Jul;2(3):123-9.

38. WISHAH RA, AL-KHAWALDEH OA, ALBSOUL AM. Impact of pharmaceutical care interventions on glycemic control and other health-related clinical outcomes inpatients with type 2 diabetes: Randomized controlled trial. *Diabetes Metab Syndr.* 2014.

39. GIANCARELLI A, DAVANOSE**.** Evaluation of Nutrition Support Pharmacist Interventions. *J Parenter Enteral Nutr,* 2014.

40. ISOM KA, ANDROMALOS L, ARIAGNO M, HARTMAN K, MOGENSEN KM et al. Nutrition and Metabolic Support Recommendations for the Bariatric Patient. *Nutr Clin Pract.* 2014.

41. GIANNÌ ML, ROGGERO P, COLNAGHI MR, PIEMONTESE P, AMATO O, et al. The role of nutrition in promoting growth in pre-term infants with bronchopulmonary dysplasia: a prospective non-randomised interventional cohort study. *BMC Pediatr.* 2014;Sep 22;14:235.

42. SÁNCHEZ AIG, DE ALMAGRO CGM, ARANZANA MC, CONTINENTE AC, HEMÁNDEZ MAC. Atención farmacéutica en pacientes con nutrición enteral. Servicios de Farmacia y Endocrinología y Nutrición. Hospital Universitario Reina Sofía. Córdoba. *Farmacia Hospitalaria*, Vol. 30. N.° 1, pp. 44-48, 2006.

43. MOUSAVI ML, HAYATSHAHI A, SARAYANI A, HADJIBABAIE M, JAVADI M. et al. Impact of clinical pharmacist-based parenteral nutrition service for bone marrow transplantation patients: a randomized clinical trial. *Support Care Cancer*. 2013 Dec;21(12):3449.

44. GALATO D, ALANO GM, TRAUTHMAN SC, VIEIRA AC. A dispensação de medicamentos: uma reflexão sobre o processo para prevenção, identificação e resolução de problemas relacionados à farmacoterapia. *Rev. Bras. Cienc. Farm*., São Paulo , v. 44, n. 3, Sept. 2008.

45. RMSTRONG EP, WANG SM, HINES LE, PATEL BV, LESLIE RS et al. Prescriber perceptions of a near real-time fax alert program for potential drug-drug interactions. *J Manag Care Pharm.* 2014 May;20(5):494-500.

46. KALYANASUNDARAM A, LINCOFF AM. Managing adverse effects and drug-drug interactions of antiplatelet agents. *Nat Rev Cardiol*. 2011 Sep 13;8(10):592-600.

47. GARCIA-CABALLOS M, RAMOS-DIAZ F, JIMENEZ-MOLEON JJ, BUENO-CAVANILLAS A. Drug-related problems in older people after hospital discharge and interventions to reduce them.*Age Ageing*. 2010 Jul;39(4):430-8.

48. NAZARI MA, MA, SALAMZADEH J, HAJEBI G, GILBERT B.The role of clinical pharmacists in educating nurses to reduce drug-food interactions (absorption phase) in hospitalized patients. *Iran J Pharm Res.* 2011 Winter;10(1):173-7.

49. ANDERSON JK, FOX JR. Potential food-drug interactions in long-term care. *J Gerontol Nurs.* 2012;Apr;38(4):38-46.

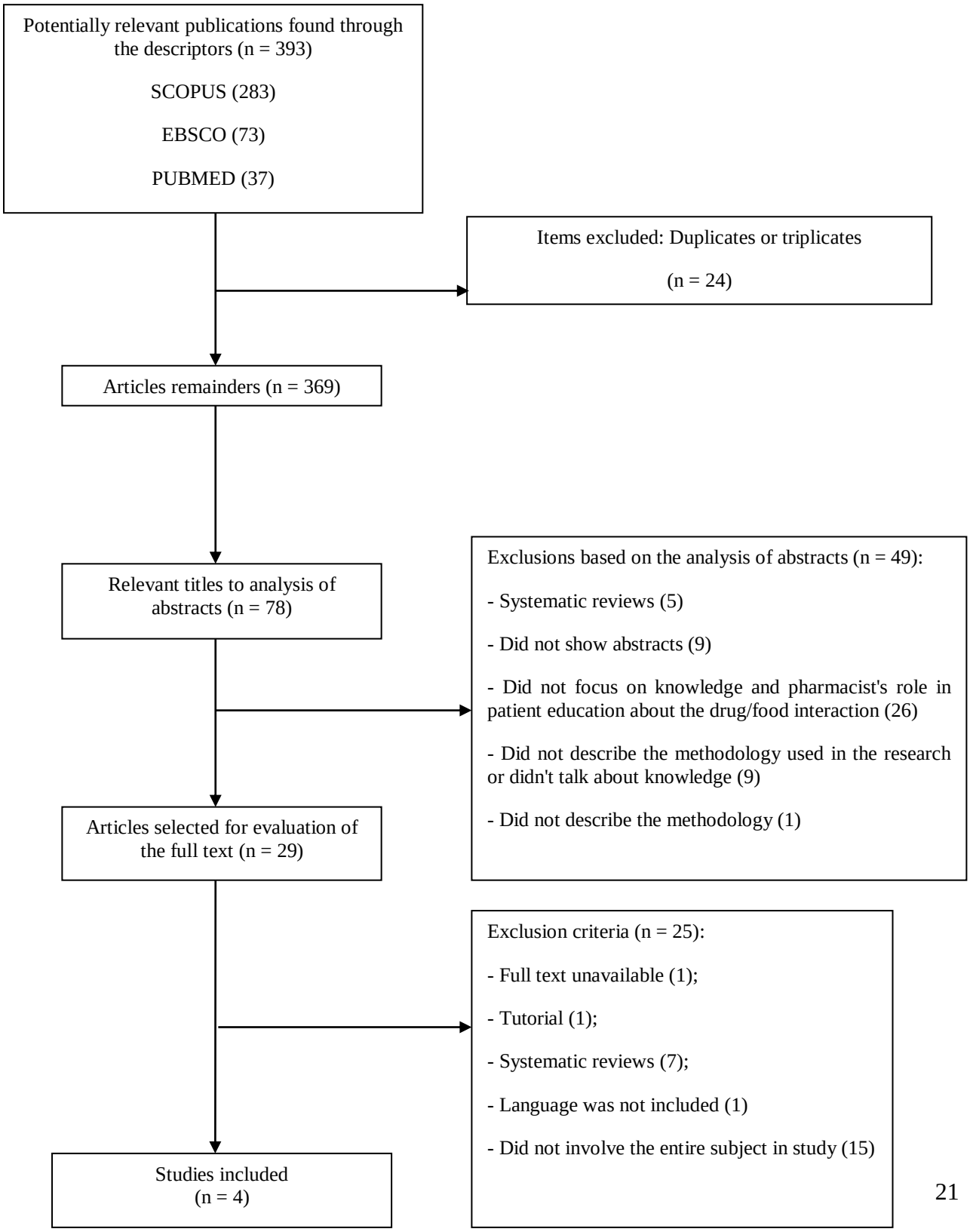
50. VON ELM E, ALTMAN DG, EGGER M, et al.; Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007; 335(7624):806-8. Available at: http://www.bmj.com/content/335/7624/806.long.

51. SHI L, HODGES M, YURGIN N, BOYE KS. Impact of dose frequency on compliance and health outcomes: a literature review (1966-2006). *Expert Rev Pharmacoeconomics Outcomes Res.* 7(2), 187-202 (2007).

52. COUTO AT, SILVA DT, SILVESTRE CC, LYRA DP Jr, QUINTANS LJ Jr. Quality analysis of research on the use of benzodiazepines by elderly patients in the emergency room: a systematic review. *Eur J ClinPharmacol.* 2013; 69(7):1343-5.

ANNEX 1

Figure 1. Flowchart of progressive selection of studies according PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses).



ANNEX 2

Table 1. General characteristics of studies (n = 4) included in the systematic review

Authors/Year	Geographic location/Setting	Study design	Patient Type	Number of patients
Miller; Raatz, 1987	United States/Hospital	NR	Patients hospitalized with a report of drug and food interactions	NR
Abbasi Nazari et al., 2010	Iran/Hospital	Interventional research	Patients hospitalized in four wards (gastrointestinal-liver; vascular surgery; endocrine and nephrology)	460
Sánchez et al., 2006	Argentina/Hospital	Prospective study	Patients admitted to hospital candidates to receive enteral nutrition	14
Cerulli; Malone, 1999	United States/Hospital	NR	Patients under the care of Clinical Nutrition Service and those receiving enteral or parenteral nutrition support	440

NR = Not Reported

ANNEX 3

Table 2. Specific characteristics of the articles (n=4) included in the systematic review

Authors/ Year	Role and knowledge of pharmacist reported	Tools to aid in the evaluation of drug-food interaction	Interaction of the pharmacist and other professionals (direct and indirect)	Pharmacist intervention in these interactions (direct and indirect)	Interventions's outcomes	Limitations
Miller; Raatz, 1987	YES	Counseling program, involving Information sheets listing nutrients affected, foods to avoid, foods to emphasize and special comments on the nutritions-related effects of the medications	Direct (pharmacists, physicians, dietitians and nurses)	Direct	A key factor in information development was maintenance of adequate nutrient intake as well as optimal drug therapy	NR
Abbasi Nazari et al., 2010	YES	Information pamphlets in which the guiding tables of drug and food usage were illustrated	Direct (pharmacists and nurses)	Indirect (The nurses' interventions were documented before and after a nurse education course supervised by a clinical pharmacist)	Incorrect consumption rate of drug regarding food in the mentioned wards fell by 13.1% after training the nurses; significant reduction of incorrect usage of drug	There are few studies about the effect of nurse education in prevention or alleviation of drug-food interactions

continued on next page

ANNEX 3

Table 2. Specific characteristics of the articles included in the systematic review *(continued)*

Authors/ Year	Role and knowledge of pharmacist reported	Tools to aid in the evaluation of drug-food interaction	Interaction of the pharmacist and other professionals (direct and indirect)	Pharmacist intervention in these interactions (direct and indirect)	Interventions's outcomes	Limitations
Sánchez et al., 2006	YES	Data collection form and a guide for drug delivery SNG.	Direct (physicians specialist in endocrinology and nutrition, nursing staff and dietitians)	Direct	The incorporation of the pharmacist in the nutritional support team helped to resolve problems in drug administration by nasogastric tube and in the evaluation and selection of the most appropriate enteral nutrition for each patient.	There are not many studies on the pharmacotherapy accomplished by pharmacists in patients with enteral nutrition in hospitals.
Cerulli; Malone, 1999	YES	Medication administration sheets were developed and sent to the patient care unit with agents that need special administration by tube.	Direct (physicians)	Direct	Drug costs were reduced; prevented and resolved problems related with drugs and improved therapeutic outcomes.	NR

NR = Not Reported

ANNEX 4

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations and reported percentages of observational studies.

Parts of article	STROBE recommendations	Reported percentage (No. reported/possible)
Title	Indicates the design of the study with terms commonly used in the title and abstract or only abstract	0% (0/4)
Abstract	The abstract provides an informative and balanced summary of what was performed and what was found	75% (3/4)
Introduction	Context/justification: Details the theoretical framework and the reasons for conducting the research	75% (3/4)
	Objectives: Presents specific objectives, including any pre-existent hypotheses.	75%(3/4)
Methods	Study design: Presents key elements regarding the study design at the beginning of the article	50% (2/4)
	Scenario: Describes the practice setting and relevant places and dates, including the period of exposure, recruitment, follow-up, and data collection.	75% (3/4)
	Participants: Cohort studies—describes inclusion criteria, data sources, and selection methods Cross-sectional studies—describes inclusion criteria, data sources, and participation selection method.	75% (3/4)
	Variables—clearly defines all results, risks, indicators, potential confounding factors, and modifying effects	0%(0/4)
	Data source/calculation—for each variable of interest, provides data sources and details on evaluation methods. Describes the evaluation of comparison methods	0%(0/4)
	Bias—specifies all measures adopted to avoid potential sources of bias	0%(0/4)
	Study size—explains how the sample size was determined	25% (1/4)
	Statistical methods—describes all statistical methods, including those used for confounding factor control. 83.3 % (5/6) Describes all methods used to examine subgroups and interactions. Explains the approach for missing data	0%(0/4)
Results	Participants: Reports the number of participants in each stage of the study; for example, the numbers of patients that were potentially eligible participants, examined for eligibility, confirmed for eligibility, included in the study, in which follow-up was completed, and included in the analysis. Provides reasons for loss in each step. Considers the use of a flowchart.	50% (2/4)
	Descriptive data: Describes the characteristics of the study participants and provides information on exposures and possible confounding factors. Indicates the number of participants with absent data for each variable of interest	75% (3/4)
	Main results: Describes the unadjusted estimates and, if applicable, the adjusted estimates by confounding variables and their precision (for example, 95 % confidence intervals). Clarifies which confounding factors were adjusted and why they were included	0% (0/4)
	Other analyses: Reports other analyses performed; for example, subgroups and interactions and sensitivity analyses	0%(0/4)
Discussion	Main results: Summarizes the main results with reference to the study objectives	75% (3/4)
	Limitations: Discusses the study limitations, considering sources of potential bias or imprecision. Discusses the direction and magnitude of any potential bias	0% (0/4)
	Interpretation: Presents a cautious interpretation of the results, considering the objectives, the limitations, the multiplicity of analyses, the results of similar studies, and other relevant evidence	75% (3/4)
	Generalization: Discusses the generalization (external validity) of the study results	0%(0/4)
	Support	0% (0/4)