CRITICAL EVENTS IN THE MAINTENANCE OF VACCINE CONSERVATION

EVENTOS CRÍTICOS NA MANUTENÇÃO DA CONSERVAÇÃO DE VACINAS

EVENTOS CRÍTICOS EN MANTENIMIENTO DE LA CONSERVACIÓN DE VACUNAS

Eliete Albano de Azevedo Guimarães¹, Valéria Conceição de Oliveira², Maila Martins Oliveira³, Selma Maria da Fonseca Viegas⁴, Ana Paula Ferreira⁵, Felícia Cristina de Souza Dias⁶

ABSTRACT

Objective: to analyze the scientific production on evidence related to the critical events in the maintenance of the cold chain of conservation of vaccines. **Method:** integrative review conducted in the period from 2011-2016. Bibliometric analysis of the selected articles was carried out in the SciELO library and in the LILACS and PUBMED/MEDLINE databases in order to answer the guiding question << What problems interfere in the quality of the maintenance of the vaccine storage cold chain? >>. **Results:** the review consisted of 24 articles, and half of the publications provided evidence of descriptive studies (level of evidence 4) and only 8.3% were classified as experimental (level of evidence 2). No articles were rated at level 1 (meta-analysis). The most cited critical events refer to insufficient training and lack of knowledge about vaccine retention, inadequate monitoring of temperature records of refrigeration equipment, and lack of supervision in the vaccine room. **Conclusion:** the critical events presented, impact the credibility of the immunization programs, making it essential to train the professionals and monitor the processes that involve the manipulation of vaccines by the supervisors of the health units and managers of the municipalities. **Descriptors:** Vaccines; Refrigeration; Immunization Programs; Health Evaluation; Nursing; Public Health.

RESUMO

Objetivo: analisar a produção científica sobre evidências relacionadas aos eventos críticos na manutenção da cadeia de frio de conservação de vacinas. **Método:** revisão integrativa realizada no período de 2011-2016. Realizou-se a análise bibliométrica dos artigos selecionados na biblioteca SciELO e nas bases de dados LILACS e PUBMED/MEDLINE com vistas a responder à questão norteadora <<Quais os problemas que interferem na qualidade da manutenção da cadeia de frio de conservação de vacina?>>. **Resultados:** a revisão constou de 24 artigos, sendo que metade das publicações trouxe evidências de estudos descritivos (nível de evidência 4) e somente 8,3% foram classificados como experimentais (nível de evidência 2). Nenhum artigo foi classificado com nível 1 (metanálise). Os eventos críticos mais citados referem-se à capacitação insuficiente e ao desconhecimento sobre a conservação de vacina, a falta de monitoramento adequado dos registros de temperatura dos equipamentos de refrigeração e a ausência de supervisão em sala de vacinas. **Conclusão:** os eventos críticos apresentados impactam a credibilidade conquistada pelos programas de imunização tornando-se fundamental a capacitação dos profissionais e o monitoramento dos processos que envolvem a manipulação das vacinas por parte dos supervisores das unidades e gestores de saúde dos municípios. **Descritores:** Vacinas; Rede de Frio; Programas de Imunização; Avaliação em Saúde; Enfermagem; Saúde Pública.

RESUMEN

Objetivo: analizar la producción científica sobre evidencias relacionadas con los eventos críticos en el mantenimiento de la cadena de frío de conservación de vacunas. **Método:** la revisión integrativa, realizada en el período 2011-2016. Se realizó la análisis bibliométrico de los artículos seleccionados en la biblioteca SciELO y en las bases de datos LILACS y PUBMED / MEDLINE, con miras a responder a la cuestión orientadora << Cuales los problemas que interfieren en calidad del mantenimiento de la cadena de frío de conservación de la vacuna?>>. **Resultados:** la revisión constó de 24 artículos, la mitad de las publicaciones aportó evidencias de estudios descriptivos (nivel de la evidencia 4) y sólo el 8,3% fueron clasificados como experimentales (nivel evidencia 2). Ningún artículo fue clasificado con nivel 1 (meta-análisis). Los eventos críticos más citados se refieren a la capacitación insuficiente y al desconocimiento sobre la conservación de la vacuna, la falta de monitoreo adecuado de los registros de temperatura de los equipos de refrigeración y la ausencia de supervisión en sala de vacunas. **Conclusión:** los eventos críticos presentados impactan en la credibilidad conquistada por los programas de inmunización, tornándose fundamental la capacitación de los profesionales y el monitoreo de los procesos que involucran la manipulación de las vacunas, por parte de los supervisores de las unidades y gestores de salud de los municipios. **Descriptor:** Vacunas; Refrigeración; Programas de Inmunización; Evaluación en Salud; Enfermería; Salud Pública.

¹PhD, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: elietalbano@ufsj.edu.br ORCID iD: <http://orcid.org/0000-0001-9236-8643>; ²PhD, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: valeria.oli.enf@gmail.com ORCID iD: <http://orcid.org/0000-0003-2606-9754>; ³Master, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: mailamartins@ufsj.edu.br ORCID iD: <http://orcid.org/0000-0002-0289-2378>; ⁴PhD, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: selmaviegas@ufsj.edu.br ORCID iD: <http://orcid.org/0000-0002-0287-4997>; ⁵Nursing student, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: anapf0@hotmail.com ORCID iD: <http://orcid.org/0000-0001-6933-1578>; ⁶Nursing student, Federal University of São João del-Rei / UFSJ. Divinópolis (MG), Brazil. E-mail: feliciasouza.9@hotmail.com ORCID iD: <http://orcid.org/0000-0003-2479-539X>

INTRODUCTION

Maintaining the vaccine storage cold chain is essential to avoid changes in the composition, potency and efficacy of immunobiological products, which are temperature sensitive products.¹ Exposure to heat reduces shelf life, while freezing causes irreversible loss of potency. Monitoring the cold chain from the producing laboratory to the vaccine room has required increasing efforts in both developed and developing countries to ensure that end users throughout the world receive effective vaccines.²

In addition to impairment of the quality of the vaccine, failures in maintaining the cold chain generates a considerable increase in the costs of the National Immunization Programs caused by the unnecessary losses of vaccines.³⁻⁴

The maintenance of the cold chain for the conservation of the immunobiological aims to protect the vaccines of inactivation for the exposure to the low or elevated temperatures, which can result in losses of the power, compromising its final effect of immunization, besides increasing the risk of adverse event post-vaccination.⁴⁻⁵

In studies carried out in several parts of the world, failures were detected that compromise the maintenance of this chain such as: lack of observation of the equipment in the temperature range recommended for the conservation of vaccines; lack of devices to monitor this temperature; insufficient procedures to receive vaccines to control the temperature at the time of vaccine arrival at the various levels of the cold chain; equipment that is worn and needs replacement.⁵⁻⁸

The Center for the Control and Prevention of Communicable Diseases (CDC), in response to various problems in the vaccine cold chain, has released a document with new recommendations for the storage and monitoring of immunobiologicals, stressing the importance of adequate maintenance of this chain. Most of the new recommendations aim to minimize exposure to accidental freezing, which is in fact the main threat to the potency of the immunobiological compromising its effectiveness.⁹

In this way, it is increasingly necessary to carry out studies on the maintenance of the vaccine conservation cold chain in order to offer the population vaccines in their maximum power state, reducing procedural failures, in order to guarantee the security. The realization of this integrative review is justified by the need to identify, gather and

synthesize the critical events that interfere in the quality of the vaccine conservation cold chain and, from this, to present solutions.

OBJECTIVE

- To analyze the national and international scientific production on the evidences related to the critical events in the maintenance of the cold chain of conservation of vaccines.

METHOD

An integrative review, based on the Evidence-Based Practice (EBP),¹⁰ which sought to aggregate and synthesize research results on a specific theme whose purpose is the synthesis of knowledge and its applicability in practice.¹¹ This study was organized considering five steps: identification of the theme and selection of the hypothesis or question of research for the elaboration of the integrative revision; establishment of criteria for the inclusion and exclusion of studies in sampling and search in the literature; definition of the information to be extracted from the selected studies / categorization of the studies; evaluation of the studies included in the integrative review and interpretation of the results.¹²

This review had as a guiding question: What are the critical events (problems) that interfere with the quality of the maintenance of the vaccine conservation cold chain? This guiding question was elaborated from the PICO strategy, which takes into account the problem, the intervention, the comparison and the expected results.¹³

The bibliographic survey was carried out by two researchers through a search in the databases: Virtual Health Library (VHL), which includes the Latin American and Caribbean Literature in Health Sciences (LILACS) databases, Database in Nursing (BDENF) and Scientific Electronic Library Online (SCIELO). A search was also made in the Medical Literature Analysis and Retrieval System Online (MEDLINE), which encompasses the Public Medline or Publisher Medline (PUBMED) database, between August and December 2016.

The descriptors were selected in the DeCS (Descriptors in Health Science) and MeSH Database. They were: vaccines, immunization, refrigeration, cold chain, immunization programs, vaccines, immunization, refrigeration, cold chain. To filter the publications relevant to the review, the descriptors were combined using the Boolean operator 'AND', as follows: immunization and refrigeration programs; vaccines and refrigeration; cold chain and vaccines;

immunization program and cold network, immunization and refrigeration programs, vaccines and refrigeration, cold chain and vaccines, immunization program and cold vaccines.

The articles published in Brazil and abroad were published in the Portuguese, English and Spanish languages, covering the period 2011-2016, in order to address the issue of vaccine conservation. The search for articles is justified as of that date due to the publication of an integrative review carried out in 2011. Exclusion criteria were the manuals, protocols and technical standards of cold stores, theses, dissertations, book chapters and articles that were outside the established research period.

The selection process of the publications is shown in Figure 1. In the first refinement of the research, we found 99 publications. Of these, 60 were excluded by repetition of the titles in the databases. From the 39 publications selected, the abstracts were read, and ten publications were excluded because they were related to the cost-effectiveness of vaccines. For the reading in full, 29 publications were selected. After reading, five articles were excluded because they did not answer the guiding question. The review consisted of a sample of 24 articles (Figure 1).

Figure 1.- Process diagram of selection of articles. Divinópolis (MG), Brazil, 2017.

The articles were analyzed in the period from February to June 2017. For the characterization of the selected publications, the bibliometric analysis of the data containing the items: year, author, origin, area of study, type of study and level of evidence (LE) to evaluate the methodological quality of the studies.

The LE analysis followed the following hierarchy proposal: evidence resulting from the meta-analysis of multiple randomized controlled trials (Level 1); evidences obtained in individual studies with an experimental design (Level 2); evidence from quasi-experimental studies, such as non-randomized studies with single pre- and post-test groups, time series or case-control (Level 3); evidence

from descriptive (non-experimental) studies or qualitative approach (Level 4); evidence from case or experience reports (Level 5); evidence based on expert opinions (Level 6).¹⁴

For the identification of the critical events in the maintenance of the cold chain of conservation of vaccines, the Donabedian dimensions of structure and process were used. The structure represents the physical, human and organizational conditions in which care is given and the process refers to the dynamics of care in services.¹⁴

Finally, the descriptive analysis of the data for the synthesis of the results of the review presented in synoptic tables.

This study was approved by the Ethics Committee in Research with Human Beings of the Federal University of São João del-Rei (CEP / UFSJ) under opinion no. 1,231,140 and CAAE 47997115.2.0000.5545.

RESULTS

The results showed that 18 (75%) of the 24 articles were published in international journals and only six (25%), published in Brazil. International publications originate from countries: Spain, Cameroon, Germany,

United Kingdom, United States, Tunisia, Ethiopia, New Zealand and India.

The number of nurses (n = 6, 25.0%), pharmacists (n = 2, 8.3%), number of nurses (n = 13, 54.2%), biomedical (n = 2, 8.3%) and a system engineer (4.2%).

Among the 24 analyzed publications, 12 (50.0%) were classified as level of evidence 4; five (20.8%) were LE 3; (16.7%), with LE 5 and one (4.2%), with LE 6. Only two (8.3%) were classified as LE 2. No publication was classified as LE 1. Most nurses published in national journals (five), two articles with LE 3 and three with LE 4. Only one of them published in an international journal with LE 2.

Figure 2 summarizes the description of the year of publication, authors, area of action, country of origin and LE.

Year	Author	Origin	Work area	Type of study	(NE) ¹
2016	Kristensen et al.	U.S	Drugstore	Descriptive	NE 4
2016	Fernández et al.	Spain	Medicine	Descriptive	NE 4
2016	Raglione et al.	Brazil	Medicine	Descriptive	NE 4
2015	Thielmann et al.	Germany	Medicine	Review	NE 5
2015	Purssell E.	United Kingdom	Nursing	Experimental	NE 2
2015	Yakum et al.	Cameroon	biomedicine	Review	NE 5
2015	Angoff et al.	U.S	Medicine	Descriptive	NE 4
2015	Oliveira et al.	Brazil	Nursing	Observational	NE 3
2014	Lloyd et al.	Tunisia	E. Biosystems	Descriptive	NE 4
2014	Som et al.	India	Medicine	Descriptive	NE 4
2014	Colloster et al	U.S	Medicine	Observational	NE 3
2014	Sachin et al.	U.S	Medicine	Review	NE 5
2014	Kartoglu et al.	United Kingdom	Medicine	Review	NE 5
2014	Oliveira et al.	Brazil	Nursing	Observational	NE 3
2013	Araújo et al.	Brazil	Nursing	Descriptive	NE 4
2013	Long et al.	U.S	Drugstore	Observational	NE 3
2013	Ateudjieu et al.	Cameroon	biomedicine	Recommendation	NE 6
2013	Asres et al.	Ethiopia	Medicine	Descriptive	NE 4
2013	Murhekar et al.	India	Medicine	Descriptive	NE 4
2013	Rogie et al.	Ethiopia	Medicine	Experimental	NE 2
2012	Vasconcelos et al.	Brazil	Nursing	Descriptive	NE 4
2012	Oliveira et al.	Brazil	Nursing	Descriptive	NE 4
2011	Mallik et al.	India	Medicine	Descriptive	NE 4
2011	Turner et al.	New Zealand	Medicine	Observational	NE 3

Note1 - LE- Level of evidence.

Figure 2. Distribution of selected articles according to: year, author, origin, area of study, type of study and level of evidence. Divinópolis (MG), Brazil, 2017

The critical events observed in the evaluation of the maintenance of the vaccine storage cold chain were analyzed according to the structural and process questions (Figure 3).

Critical events	Articles	
	n	%
Structure		
Non-exclusive room for vaccination.	2	8.3
Non-exclusive use of the vaccine cooler.	3	12.5
Lack of material resources: thermal box, coils and thermometers.	3	12.5
Lack of functional refrigerators in units.	4	12.5
Absence of daily temperature control map with records.	2	8.3
Insufficient training of the staff working in the vaccine room.	5	62.5
Inadequate logistics for the distribution of vaccines.	4	16.7
Process		
Absence of supervision in the vaccine room.	5	20.8
Faults in the maintenance of the cold grid due to grid instability.	3	12.5
Preventive maintenance of cold chain equipment.	1	4.2
Accidental freezing during storage.	2	8.3
Lack of proper monitoring of temperature records of refrigeration equipment.	10	41.7
Defrosting and cleaning of refrigeration equipment outside recommended standards.	2	8.3
Failure to adhere to the standards and recommended guidelines.	1	4.2
Failure of actions of epidemiological surveillance and health education.	2	8.3
Absence of communication to the higher instance of temperature changes.	1	4.2
	8	33.3

Figure 3. Frequency of critical events related to the maintenance of the vaccine storage cold chain according to the structure and process dimensions. Divinópolis (MG), Brazil, 2017.

Regarding structural issues, the most cited event was insufficient training of the staff working in the vaccination ward, followed by inadequate logistics for the distribution of vaccines. The lack of proper monitoring of temperature records of refrigeration equipment, insufficient staff knowledge about vaccine retention, and lack of vaccine room supervision were the most frequent critical events in the vaccine retention process.

DISCUSSION

Analyzing the incorporation of evidence in the studies implies determining the confidence of the results found and strengthening the conclusions that will generate the state of the current knowledge of the researched subject. The classification of the articles regarding LE is a challenge due to the lack of clarity in the description of the methodological path of the studies.¹³ This challenge was corroborated in most of the articles found evidencing fragilities in the description of the methods, including in international articles with higher LE.

Few articles were published in Brazil and, mostly, by nurses. In the Brazilian public services, the activities developed in the vaccination room are still specific to Nursing professionals.¹ However, Abroad, scientific production was restricted to non-nurses since they do not routinely assume responsibility for immunization services.⁹

In the area of Nursing, few studies with higher levels of evidence have been found, which presupposes that the nurse has not yet appropriated this methodology for conducting the research on the cold chain of vaccine conservation. The results showed that most of

the studies are descriptive and point to the diagnosis of vaccine conservation without, however, making interventions to improve the quality of the service provided. In this aspect, it is urgent to include experimental methods in Nursing research to ensure greater impact of their results.

The insufficient training of the staff working in the vaccine room was reported in most articles investigated.^{3,6,8,15-20} Studies conducted in Brazil and abroad show that many professionals are unaware of basic standards such as the appropriate temperature for the conservation of vaccines,^{4,7,16,21} essential item for the adequate conservation of the immunobiological and that evidences failures in the qualification of the team in the vaccine room. Periodic assessment, continuing and continuing education, and response to training requirements, such as team motivation, help to address this reported hurdle.

In Brazil, it was identified that the training of the staff working in the vaccine room is not carried out in a systematic and continuous way, it is aimed at the technical-scientific update and, most of the time, it is offered by the technical references in municipal and state immunization when of the changes in the PNI.²⁰ It is important to emphasize that education must be permanent, based on the needs of professionals working in the vaccination rooms, in order to improve skills, reducing the frequency of critical events and, consequently, raising quality of the assistance.¹⁸

In order to ensure immunobiological efficacy and safety of vaccines, it is necessary to maintain adequate refrigeration equipment and in optimum operating conditions.

Currently, it is recommended to replace household type refrigerators with refrigerated chambers.^{4-5,22-3} These chambers, when compared to domestic refrigerators, keep the temperature stable and homogeneous throughout the equipment, reducing the risk of exposure of immunobiologicals to changes in temperature outside the recommended parameter.^{1,24}

Most vaccination rooms do not yet have this equipment available.^{18,22,25} Such a situation may compromise the safety of immunobiological conservation since the household refrigerator does not maintain a homogeneity in temperatures and does not prevent the freezing of vaccines.⁴⁻⁵ In addition, in Brazil, Cameroon, India, New Zealand and Ethiopia, irregularities were detected in the storage, cleaning and operation of domestic refrigerators.^{6,25,26-8}

Inadequate logistics in the distribution of vaccines was another critical factor in maintaining the vaccine conservation cold chain identified in the articles analyzed. In a study carried out in India, it was found that, during the transport of the vaccines from the state to the local instance, they were frequently exposed to temperatures below or higher than the recommended values.²⁹⁻³⁰

During transport of vaccines, there is a need for temperature monitoring with regularly calibrated devices,^{4,25,31} in addition to effective visual inspection to identify any exposure to freezing temperatures.⁹ Continuous temperature monitoring during transport increases the likelihood to identify occurrences of exposure to freezing temperatures compared to the less strict control.⁹

One of the solutions to ensure transport safety is the replacement of recyclable ice packs by the use of cold water packs without causing any damage to the potency of the vaccines. The World Health Organization's new performance, quality and safety specifications bring clarity to the issue and recommend the use of only cold water packs for vaccines sensitive to freezing.²² Another solution would be the production of thermostable vaccines reducing dependence on the cold chain and impacting the stability and potency of vaccines.^{21,24,32}

Not only during transport, but also during the storage of vaccines, it is necessary to strictly monitor temperatures with measuring equipment such as thermometers. The lack of such monitoring was identified in almost half of the analyzed articles, which could compromise the quality, efficiency and effectiveness of the vaccine. It is important to

note that, in addition to the thermometers, the datalogger is currently the recommended measuring instrument since it is possible to know all temperature exposures (especially the lowest ones) during long weekends and holidays.^{5,9,21-3}

In addition to the datalogger, visual freezing indicators are useful in early identification of freezing events involving vaccines. Consideration should be given to including such devices as a component of the vaccine temperature monitoring system.³³

The stability of the electric network is another necessary item for the proper maintenance of the cold chain. It has been documented in a study in Nigeria that the irregular supply of electricity in health facilities and the absence of a backup generator were major risk factors for loss of vaccine potential.²⁸

Ensure that each vaccine room, or health facility where vaccination occurs, has at least one backup source other than the primary source is a viable solution that can ensure the efficiency and effectiveness of maintaining the cold chain. Currently, there is a generator model that can be coupled to the refrigeration chamber and has a low financial cost.^{7,21,23,25,31}

In this review, it was evidenced that the supervision is an important recommendation for the conservation of the immunobiologicals to be made in a safe and with quality. The supervision of the vaccine room should be continuous and systematic with planning, direction and organization, being the professional attentive if the activities carried out are in accordance with the recommended norms.^{18,20}

Supervision provides the nurse or other responsible professional with critical insight into the team's difficulties and the demand for training according to the problems encountered.¹⁸ Through systematic supervision, the health professional can guide, support and assist the team improving the performance of professionals and, consequently, making them more competent. However, in order to exercise supervision, in addition to supervisors' knowledge about immunization, it is relevant to learn in the area of management using specific tools for this purpose.^{18,34}

Significant improvements can be made to the management of the cold chain resulting in less waste of vaccines and ensuring efficient immunobiologicals. In a study conducted in New Zealand, this was demonstrated over a period of six years and was attributed to several factors such as: improved equipment;

permanent education and training systems; attention to quality standards of the cold chain and strict observation in the transport of vaccines to primary care.²⁹

Given the importance of the conservation of vaccines, it is relevant to carry out studies that evaluate the adherence of the responsible team to the technical standards of vaccine conservation. And, the evaluation in the daily life of the services strengthens and / or develops the technical qualification to adopt the monitoring and evaluation actions pertinent to planning and management as an instrument to support the formulation of policies, the decision making process and the training of professionals.³⁵

Among the limitations of this study, it was evidenced that, in relation to the outline of the reviewed articles, the majority had low level of evidence, which can impact the ownership of the knowledge produced and its applicability in practice. Differences were also identified regarding the professional category of the person in charge of the vaccine room, which made it difficult to generalize the results found.

CONCLUSION

The critical events presented impact the credibility that the immunobiological ones have been conquering in the last decades becoming fundamental the orientation of the professionals and the monitoring of the processes that involve the manipulation of these substances by the supervisors of the units and health managers of the municipalities.

Likewise, the importance of the elaboration and validation of an instrument that makes it possible to evaluate the conservation of vaccines is undoubtedly important, since the maintenance of the cold chain ensures the immunogenic characteristics from the production to the administration of the vaccine. This review provided a theoretical basis for the elaboration of an instrument to evaluate the cold chain to be validated later.

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Corresponding Address

Eliete Albano de Azevedo Guimarães
Rua Sebastião Gonçalves Coelho, 400
Bairro Chanadour
CEP: 35501-296 - Divinópolis (MG), Brazil