Algorithm Formalization for Decision Making in Influenza Vaccination

Enrique Monsalvo San Macario^{a,b}, Marta Fernández Batalla^{a,c}, Alexandra González Aguña^a, José María Santamaría García^{a,c}, Adriana Cercas Duque^{a,d}, Virginia Díaz Teruel^{a,e}, Blanca Gonzalo de Diego^{a,c}, Sara Herrero Jaén^{a,f}, Diego Cobo González^{a,g}

^a Research Group MISCK (Alcala University), Alcalá de Henares, Spain
^b Health Center La Garena, Alcalá de Henares, Spain
^c Health Center Meco, Meco, Spain
^d La Zarzuela Hospital, Madrid, Spain
^e 12 de Octubre Hospital, Madrid, Spain
^f Severo Ochoa Hospital, Leganés, Spain
^g La Paz Hospital, Madrid, Spain

Abstract

Influenza is an important public health problem with consequences on the health of people, but also at the state level with social and health costs due to the morbidity and mortality produced. Vaccination is an act of care of high clinical complexity, which can be learned and trained, so that decisionmaking in vaccination requires elements of judgment that act logically in a cascade. The creation of algorithms and their implementation in computer systems will identify susceptible people more quickly and improve the competence in the administration of vaccines. For the creation of the algorithm, the variables and their relationships were identified through mathematical formulation. As a result, the nine variables for vaccination that result in 47 different clinical situations were identified (29 "non-vaccination" and 18 "vaccination" situations). The formalization of algorithms in vaccine administration allows to represent the process by which the professional carries out the decision making process.

Keywords:

Algorithms; Decision Support Systems, Clinical; Influenza Vaccines

Introduction

The present study starts from the following reseach aim: to design an algorithm that describes the decision-making process in influenza vaccination. Influenza is an acute respiratory infection caused by RNA-virus that encompasses different groups (mainly groups A, B and C) with type A being the most prevalent [1]. This infection appears in the form of epidemic outbreaks and because of the high rate of virus mutation (especially H3N2) [2], annual vaccination is necessary (with an effectiveness of 70-90% if there is concordance between the strains) [3,4]. The virus is transmitted by air, and transmission period may begin from one day before the symptomatic phase to seven days after symptoms start [5]. Influenza is characterized by high fever, cough, muscle and joint pains, headacheand and intense discomfort. In people with poor health, the flu and its complications can be fatal, due to pneumonias caused by secondary bacterial invaders [1].

Worldwide, influenza accounts for about 300,000 to 600,000 seasonal influenza-associated respiratory deaths annually [2]. In Spain, the flu surveillance report indicates that 5,977 severe hospitalized confirmed cases of influenza were reported, of

which 21.8% were admitted to the ICU and 17.3% died in the 2017/2018 season [6]. In the Community of Madrid, an accumulated incidence of 1,540.33 cases per 100,000 inhabitants was estimated in the same season [7]. In conclusion, influenza is a major public health problem worldwide related to a high rate of morbidity and mortality, increase in social and health costs, potentially preventable and whose management and control of risk should continue to evolve and improve to increase the level of health of the community [2,7].

Vaccination is one of the main acts of care in primary prevention, definid as health behaviors aimed at avoiding the health problem, or reducing the probability of it appearing [8]. In particular, it is essential for the prevention of health problems of infectious origin worldwide [9]. Fernandez Batalla et al. indicate that vaccination is an act of care of high clinical complexity, which can be learned and trained, so that decisionmaking in vaccination requires elements of judgment that act logically in a cascade. The first assessment should be based on the characteristics of the individual (vaccine selection) and then the administration decision according to the context [10]. In addition, the computational implementation of decisionmaking in care allows a better identification of the population to which vaccination is recommended. This allowed us to design tools for specific distance recruitment and increase vaccination rates, which has been progressively decreasing in recent years [11].

Methods

For the identification and description of variables, the methodology used was deductive, based on:

- Extraction of knowledge through text analysis
 - Scientific and technical regulations of the Public Health services, in relation to the indication of influenza vaccination for the 2017-2018 influenza campaign of the Community of Madrid.
 - Instructions for use and technical data sheets of the influenza vaccines available in said campaign.
- Education throught expert's knowledge.

The expert group consists of a nurse doctor in computer science, mathematical doctor in computer science, a nurse specialist in community health, and two master's degree nurses in multidisciplinary informatics.

Establishment of existing relationships between variables: algorithm creation.

 Mathematical formulation through bivalued logic: Identification of relevant clinical variables and definition of possible values for each variable[12-14].

Results

Extraction and Definition of the Variables.

A total of 9 variables relevant to influenza vaccination were selected.

Age

Time a person has lived at the time of the valuation. It was classified into 6 stages: less than 6 months (e0), 6 - 35 months (e1), 3 - 8 years (e2), 9 - 59 years (e3), 60 - 64 years (e4) and 65 years or more (e5).

Life Process

Indicates the presence of factors that indicate risk group for vaccination. Three main groups were identified:

- Processes that increase the risk of complications from the flu
- People who can pass the flu to those who are at high risk of complications
- Essential public service workers

With the presence of one factor it will be considered posive (r) while the absence of all of them will be considered negative $(\neg r)$

First Vaccination

Indicates that the person has not been vaccinated against the flu in previous years (p).

Interval Between Doses

When vaccination with several doses is necessary, it indicates that 4 weeks have passed after the first dose (i).

Initial Dose

When vaccination with several doses is necessary, it indicates that the vaccine proposed constitutes the first dose to be administered in this anti-flu campaign.

Influenza Vaccination Completed

Indicates the correct vaccination in the current anti-flu campaign (c)

Health Situation

Indicates the presence of factors that contraindicate the administration of the vaccine at that time. Three main situations were identified: fever, acute infection, allergy to some components of the vaccine.

With the presence of one factor it will be considered posive (s) while the absence of all will be considered negative (\neg s).

Anticoagulation

Indicates that the patient is at increased risk of hemorrhage by intramuscular puncture (a).

Vaccination Action

It is the result variable. Indicates whether the vaccine is indicated (v) or not (\neg v) and complementary information (type of vaccine, dose, route of administration, cause of non-vaccination).

Order of Variables

For decision making in vaccination, a hierarchy of the variables is necessary to indicate when to ask for each variable.

The final formalization of the variables is presented in Table 1.

Tablal	Dogowinstion and	E anna ali- ation	of Vaniahlaa
Table I - I	Description and	rormalization	of variables

Variable	Order	Code	Range
Age	1	e	e0 –e5
Life process	2	r	r/¬r
Influenza vaccination completed	3	c	c/¬c
First vaccination	4	р	p/¬p
Initial dose	5	d	d/¬d
Interval between doses	6	i	i/¬i
Anticoagulation	7	а	a/¬a
Health situation	8	s	s/¬s
Vaccination action	9	v	$v / \neg v$

Establishment of the Relationships Between Variables

With the identified variables, a total of 47 different clinical cases were obtained leading to a specific vaccination action (Table 2).

- 29 "non-vaccination" situations. The algorithm has five different causes that indicate "no vaccination" (distribution in Figure 1).
- 6 situations in which to vaccinate with inactivated vaccine (0.25ml)
- 11 situations in which to vaccinate with inactivated vaccine (0.5ml)
- 1 situation in which to vaccinate with inactivated vaccine with adjuvant (0.5ml)

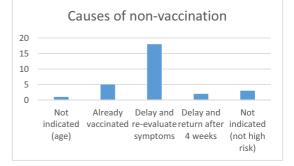


Figure 1 – Distribution of Reasons for Non-Vaccination

Table 2 - Coding of the Algorithm

	-	
Caso clínico		Acción vacunal
e0	\rightarrow	¬v1
el Ar A c	\rightarrow	¬v2
e1 ∧ r ∧ ¬c ∧ p ∧ d ∧ a ∧ s	\rightarrow	v3 ∧ ¿s?
$e1 \land r \land \neg c \land p \land d \land \neg a \land s$	\rightarrow	¬v4 ∧ ¿s?
el∧r∧¬c∧p∧¬d∧i∧a∧s	\rightarrow	¬v5 ∧ ¿s?
e1 ∧ r ∧ ¬c ∧ p ∧ ¬d ∧ i ∧ ¬a ∧ s	\rightarrow	¬v6 ∧ ¿s?
$e1 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge \neg i$	\rightarrow	¬v7 ∧ ¿i?
$e1 \wedge r \wedge \neg c \wedge \neg p \wedge a \wedge s$	\rightarrow	¬v8 ∧ ¿s?
$e1 \wedge r \wedge \neg c \wedge \neg p \wedge \neg a \wedge s$	\rightarrow	¬v9 ∧ ¿s?
e1∧¬r	\rightarrow	¬v10
e2 A r A c	\rightarrow	¬v11
$e2 \land r \land \neg c \land p \land d \land a \land s$	\rightarrow	¬v12 ∧ ¿s?
$e^2 \wedge r \wedge \neg c \wedge p \wedge d \wedge \neg a \wedge s$	\rightarrow	¬v13 ∧ ¿s?
$e^2 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge a \wedge s$	\rightarrow	¬v14 ∧ ¿s?
$e^2 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge \neg a \wedge s$	\rightarrow	¬v15 ∧ ¿s?
$e^2 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge \neg i$	\rightarrow	¬v16 ∧ ¿i?
$e^2 \wedge r \wedge \neg c \wedge \neg p \wedge a \wedge s$	\rightarrow	¬v17 ∧ ¿s?
$e^2 \wedge r \wedge \neg c \wedge \neg p \wedge \neg a \wedge s$	÷	¬v18 ∧ ¿s?
$e^2 \wedge \neg r$	÷	¬v19
$e^{3} \wedge r \wedge c$	÷	¬v20
$e^{3} \wedge r \wedge \neg c \wedge a \wedge s$	÷	¬v21 ∧ ¿s?
$e^{3} \wedge r \wedge \neg c \wedge \neg a \wedge s$	÷	¬v22 ∧ ¿s?
e3 ∧ ¬r	÷	-v23
$e4 \wedge c$	${\rightarrow}$ ${\rightarrow}$	¬v24
$e4 \wedge r \wedge \neg c \wedge a \wedge s$	÷	¬v25 ∧ ¿s?
$e4 \wedge r \wedge \neg c \wedge \neg a \wedge s$	÷	¬v26 ∧ ¿s?
e5 A c	\rightarrow	¬v27
$e^{5} \wedge r \wedge \neg c \wedge a \wedge s$	÷	¬v28 ∧ ¿s?
$e^{5} \wedge r \wedge \neg c \wedge \neg a \wedge s$	\rightarrow	¬v29 ∧ ¿s?
$e1 \wedge r \wedge \neg c \wedge p \wedge d \wedge a \wedge \neg s$	\rightarrow	v1
-	\rightarrow	v1 v2
$e1 \wedge r \wedge \neg c \wedge p \wedge d \wedge \neg a \wedge \neg s$	$\stackrel{\prime}{\rightarrow}$	v2 v3
$e1 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge a \wedge \neg s$	$\stackrel{\prime}{\rightarrow}$	v3 v4
$e1 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge \neg a \wedge \neg s$	$\stackrel{\prime}{\rightarrow}$	v4 v5
el $\land r \land \neg c \land \neg p \land a \land \neg s$	$\stackrel{\prime}{\rightarrow}$	v5 v6
$e1 \wedge r \wedge \neg c \wedge \neg p \wedge \neg a \wedge \neg s$	\rightarrow	vo v7
$e^2 \wedge r \wedge \neg c \wedge p \wedge d \wedge a \wedge \neg s$	\rightarrow	
$e^2 \wedge r \wedge \neg c \wedge p \wedge d \wedge \neg a \wedge \neg s$		v8
$e^2 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge a \wedge \neg s$	て、	v9
$e^2 \wedge r \wedge \neg c \wedge p \wedge \neg d \wedge i \wedge \neg a \wedge \neg s$	${\rightarrow}$	v10
$e^2 \wedge r \wedge \neg c \wedge \neg p \wedge a \wedge \neg s$	${\rightarrow}$	v11
$e^2 \wedge r \wedge \neg c \wedge \neg p \wedge \neg a \wedge \neg s$	${\rightarrow}$	v12
$e^3 \wedge r \wedge \neg c \wedge a \wedge \neg s$	\rightarrow	v13
$e^3 \wedge r \wedge \neg c \wedge \neg a \wedge \neg s$	${\rightarrow}$	v14
$e4 \wedge \neg c \wedge a \wedge \neg s$	\rightarrow	v15
$e4 \land \neg c \land \neg a \land \neg s$	\rightarrow	v16
$e5 \land \neg c \land a \land \neg s$	\rightarrow	v17
$e5 \land \neg c \land \neg a \land \neg s$	\rightarrow	v18

Discussion

In relation to the use of Information and Communication Technologies, the CDC indicates logic specification for ACIP Recommendations in Clinical Decision Support for Immunization (CDSi). The variables used in this research work resemble the variables defined by the CDC (Target dose, patient series)[15].

In the context of primary health care, Martín-Ivorra indicates that the development of this type of tools would improve to identify the people of being vaccinated who attend the scheduled consultations in Primary Care[16]. On the contrary, it has found different publications that indicate that the use of ICTs are useful to determine and increase vaccination coverage[17,18].

Gerard et al. developed a system of influenza vaccination reminders in a hospital's information systems to increase the rate of influenza vaccination in patients hospitalized in internal medicine. Although the system was effective, it did not discriminate the indication of the vaccine based on their clinical features[19]. In relation to decision making in vaccines, Jacobson describe the development, of a software tool, introduced to assist health care professionals and public health administrators in managing pediatric vaccine purchase decisions and making economically sound formulary choices[20]. In relation to the methodology, Shiffman and Greenes used this methodology with with logic and decisiontable techniques to improve cinical guidelines applicates to prevention of perinatal transmission of hepatitis B by immunization[12].

Conclusions

The formalization of algorithms in the vaccination allows to represent the process by which the professional carries out the decision making process, in this case, in the influenza vaccination. In addition, the algorithms serve as a guide for the professional. The hierarchy of variables is not the most computationally efficient but it represents in a better way the process of decision making. To measure progress in vaccination decision-making training, it is proposed to incorporate a case generator into the application in the future. Thanks to the development of the algorithm, all the variables have been coded to generate these cases.

Acknowledgements

This study was not financed by public or private company. Management about Information and Standard Knowledge of Care Research (University of Alcala) supported this work.

References

- C. J. Woolverton, J. M. Willey, and L. M. Sherwood, Microbiología de Prescott, Harley y Klein, 7th Edition, McGraw-Hill-Interamericana, España, 2013.
- [2] Lancet, Editorial. Preparing for seasonal influenza, The Lancet 391(10117), 2018.
- [3] A. Domarus, C. Rozman, and P. F. Valentí. *Medicina interna*. 17th Edition, Elsevier Health Sciences Spain, Barcelona, 2012.
- [4] World Health Organization (WHO). Vacunas antigripales: Documento de posición de la OMS, (2012) <u>http://www.who.int/immunization/position_papers/WHO</u> <u>PP_Influenza_Nov_2012_Spanish.pdf?ua=1</u>
- [5] I. Hernández-Aguado, A. Gil de Miguel, M. Delgado Rodríguez, F. Bolúmar Montrull, F. G. Benavides, and M. Porta Serra, *Manual de Epidemiología y Salud Pública para grados en ciencias de la salud. 2nd Edition*, Médica Panamericana, Madrid, 2012.
- [6] Instituto de Salud Carlos III. Informe de Vigilancia de la Gripe en España. Temporada 2017-2018, (2016). <u>http://vgripe.isciii.es/documentos/20172018/InformesAnua</u> <u>les/Informe_Vigilancia_GRIPE_2017-2018_27julio2018.pdf</u>
- [7] Servicio de Prevención de la Enfermedad. Dirección General de Salud Pública. Vacunación frente a la Gripe estacional 2018-2019, Technical document, (2018)
- [8] L. Mazarrasa Alvear, Salud pública y enfermería comunitaria, 2nd Edition, McGraw-Hill Interamericana de España, 2003.

- [9] A. Martín Zurro, Atención Primaria: conceptos, organización y práctica clínica, 6th Edition, Elsevier, 2008.
- [10] M. Fernández Batalla, M. L. Jiménez Rodríguez, J. M. Santamaría García, J. L. Gómez González, A. González Aguña, and E. Monsalvo San Macario. Conceptualización de la toma de decisiones en el cuidado: acercamiento desde la vacunación. *ENE, Revista de Enfermería*, 9(3) (2015).
- [11] Ministerio de Sanidad Servicios Sociales e Igualdad. Evolución coberturas de vacunación antigripal en población ≥ 65 años. España, temporadas 2006-2007 a 2015-2016. <u>http://www.msssi.gob.es/profesionales/saludPublica/prevP</u>

romocion/vacunaciones/docs/CoberturasVacunacion/Tabla 10.pdf 1. P. N. Shiffman, and P. A. Grannes, Improving clinical

- [12] R. N. Shiffman, and R. A. Greenes, Improving clinical guidelines with logic and decision-table techniques: application to hepatitis immunization recommendations, Med Decis Making, 14(3)(1994),245-254.
- [13] M. L. Jiménez Rodríguez. Sistema Basado en el Conocimiento para ayuda en el diagnóstico del cansancio del desempeño del rol de cuidador. PhD. University of Alcalá de Henares, Madrid, Spain. 2006.
- [14] B. Gonzalo de Diego. S. Herrero Jaén, E. Monsalvo San Macario, L. Madariaga Casquero, M. L. Jiménez Rodríguez, J. M. Santamaría García, et. al. *Robotic Implementation of the Necessary Mechanism for the Human Characteristics Simulation: Approach from Self-Care Conceptual Modeling*. Stud Health Technol Inform. 2018;250:115-120.
- [15] National Center for Immunization and Respiratory Disease (NCIRD), Immunization Information Systems Support Branch (IISSB). Clinical Decision Support for Immunization (CDSi): Logic specification for ACIP recommendations, (2019). https://www.cdc.gov/vaccines/programs/iis/interopproj/downloads/logic-spec-acip-rec-4.0.pdf
- [16] Martín-Ivorra R, Alguacil-Ramos AM, Lluch-Rodrigo JA., Pastor-Villalba E, Portero-Alonso A. Actividades para captar y vacunar a la población susceptible en la Comunidad Valenciana. Rev. Esp. Salud Pública 2015 89(4): 419-426.
- [17] I. N Souza Interaminense, S. Costa de Oliveira,L. Pedrosa Leal, F. M. Pereira Linhares, M. Pontes Cleide. Educational technologies to promote vaccination against human papillomavirus: integrative literature review, (2016). 25(2). http://www.eciela.ph/aciela.ph/2007/014750.

 $\label{eq:http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0\\ 104-07072016000200502&lng=en.$

- [18] Pastor Villalba E, Cremades Bernabeu A, Alguacil Ramos AM, Martin Ivorra R, Portero Alonso A, Lluch Rodrigo JA et al. *Recaptación activa de la 1a y 2a dosis de* triple vírica en la comunidad valenciana. Utilización y rendimiento de la herramienta del Sistema de Información Vacunal (SIV). 60 Congreso de la Asociación Española de Vacunología 23 al 26 de Nov 2011. Santiago de Compostela: Asociación Española de Vacunología; 2011.
- [19] M. N. Gerard, W. E. Trick, K. Das, M. Charles-Damte, G. A. Murphy, I. M. Benson. Use of clinical decision support to increase influenza vaccination: multi-year evolution of the system. J Am Med Inform Assoc. (2008), 15(6):776-9.
- [20] S. H. Jacobson, and E. C. Sewell, A Web-based Tool for Designing Vaccine Formularies for Childhood Immunization in the United States, J Am Med Infor Asoc, 15(5), (2008), 611-619.

Address for correspondence

Enrique Monsalvo San Macario Research Group MISKC University of Alcalá. Alcalá de Henares, Madrid (Spain). Email: <u>enrique.monsalvo@hotmail.com</u>