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SOCIEDAD ESPAÑOLA DE FARMACIA HOSPITALARIA

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Adaptación y validación del Global Trigger Tool para Pacientes Mayores Crónicos con Multimorbilidad

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sefh
Sociedad Española de Farmacia Hospitalaria

. Objetivo:

Detallar el proceso metodológico para adaptar y validar el Global Trigger Tool (GTT) para su uso en el subgrupo específico de **pacientes mayores crónicos con multimorbilidad**, resaltando los desafíos y las soluciones implementadas.

¿Qué es el TRIGGER-CHRON?

Es un listado de señales alertantes (SA) adecuadas y eficaces, para detectar eventos adversos a medicamentos (EAM) en **pacientes mayores crónicos con multimorbilidad**.

TRIGGER-CHRON

Proyecto Financiado:

- Instituto de Salud Carlos III (fondos FEDER). N° de Expediente PI15/01616.
- Grupos de trabajo de la SEFH.

Objetivos del proyecto TRIGGER-CHRON

- **Identificar** las distintas señales alertantes para la detección de EAM en pacientes adultos disponibles en la literatura científica.
- **Seleccionar,** mediante un panel de expertos, las señales alertantes teóricamente **más adecuadas** para detectar EAM en pacientes mayores crónicos con multimorbilidad.
- **Evaluar la capacidad predictiva** de cada una de las señales alertantes en la detección de EAM.
- Determinar las señales alertantes más implicadas en la detección de EAM que presentan los pacientes mayores crónicos con multimorbilidad **durante la hospitalización**.
- Identificar las señales alertantes más útiles para detectar los EAM causados por cada uno de medicamentos de alto riesgo incluidos en la **lista MARC**.

Fases del proceso metodológico

1
- Búsqueda bibliográfica: Selección de las SA que detectan EAM
- Selección de los expertos para el panel
- Evaluación de las SA por el panel de expertos

2
- Evaluación de la utilidad de las SA seleccionadas

3
- Elaboración de la lista de las SA definitiva (TRIGGER-CHRON)

4
- Selección de las SA más eficientes para detectar EAM incluidos en la lista MARC

Metodología: Delphi modificado.

1. Búsqueda bibliográfica: Selección de las SA que detectan EAM
2. Selección de los expertos para el panel
3. Evaluación de las SA por el panel de expertos

Development of a Trigger Tool to Identify Adverse Drug Events in Elderly Patients With Multimorbidity

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Purpose: Elderly patients with multimorbidity are especially vulnerable to adverse drug events (ADEs) and had high prevalence rates. Identifying ADEs is essential for enabling timely interventions that can mitigate the adverse events detected and for developing targeted strategies to prevent their occurrence as well as to monitor implementation. The aim of this study was to develop a set with appropriate triggers for detecting potential ADEs in elderly patients with multimorbidity.

Methods: A modified Delphi methodology was used to reach consensus. Existing triggers for detecting ADEs in adult patients were identified from a literature search in several databases (EMBASE, MEDLINE, Web of Science, Centre for Reviews and Dissemination, and Cochrane Library) and from Institute for Healthcare Improvement published lists. Twelve experts in patient/medication safety or in chronic diseases scored candidate triggers for appropriateness according to 3 criteria (evidence, usefulness for elderly patients, and feasibility of implementation in clinical practice).

Results: Seventy-two triggers were initially selected to be evaluated. The final set includes a total of 51 triggers for which the panelists who completed the 2 rounds of evaluation reached agreement. These triggers were organized into 5 modules: 11 as care module triggers, 10 as antidotes/treatment, 11 medication concentrations, 18 abnormal laboratory values, and 1 as emergency department trigger.

Conclusions: A set of triggers for detecting ADEs in elderly patients with multimorbidity have been developed, following the consensus of a panel of experts. Subsequent validation in clinical practice is needed to confirm the accuracy and efficiency of these triggers for this population.

Key Words: chronic patient, drug related side effects and adverse reactions/diagnosis, multi morbidity, patient safety

(*J Patient Saf* 2017;00: 00–00)

complications[2,3] and affect 4.7%[4] or even 14.7%[5] of hospitalized patients, prolonging their hospital stays. Adverse drug events occur fairly frequently as well during transitions of care, accounting for two thirds of all events experienced by discharged patients.[6] In outpatient settings, a summary report on related studies indicates that ADEs cause between 0.3% and 20.2% of visits to emergency departments and between 2.4% and 6.7% of hospital admissions.[7] It should be also noted that according to a meta-analysis,[8] approximately half of ADEs are preventable among both inpatients and outpatients.

Patient-related increased risk factors for experiencing ADEs are number of drugs taken regularly, age, and comorbidities.[9] Hence, older adults with chronic diseases are especially vulnerable to ADEs and have higher ADE prevalence rates compared with other age groups.[1] For example, statistical data from U.S. indicate that older adults (age ≥ 65 years) accounted for 35% of all hospital stays while, at the same time, accounted for 53.1% of hospital ADEs.[4] In the outpatient setting, older adults have a rate of ADEs requiring primary care or emergency department visits 2 to 3 times higher than younger persons[10,11] and are 3 to 7 times more likely to be hospitalized for ADEs.[12,13]

Both detection and characterization of ADEs, and especially of those ADEs classified as preventable, are essential for developing effective and targeted strategies to prevent their occurrence and thus improve patient safety. Various methods for identifying ADEs and medication errors have been proposed, including chart review, voluntary reporting by healthcare professionals, and direct observation, each one with its own characteristics, strengths, and limitations.[14,15] To obtain a comprehensive picture of medication safety within an organization, more than 1 identification method should be applied.[16]

The trigger tool methodology was developed to increase the efficiency of conventional chart review in the identification of ADEs, because this method is considered the criterion standard because of

BÚSQUEDA BIBLIOGRÁFICA

BBDD: EMBASE, MEDLINE (pubmed), WOS, CRD, Cochrane library, IME (1990 - mayo 2015).

Estrategia de búsqueda: pregunta PICO

Población	Pacientes adultos.
Intervención	Aplicación de las señales alertantes de medicamentos.
Comparadores	Práctica habitual (revisión de historias, notificación voluntaria, etc.)
Outcomes/ resultados	Distintas señales alertantes aplicables a la población de estudio, utilidad y valor predictivo positivo de cada una de las señales alertantes.

Review of Information and Selection of Indications

The literature review includes a total of 261 articles (46 in EMBASE, 42 in MEDLINE, 150 in Web of Science, 5 in Centre

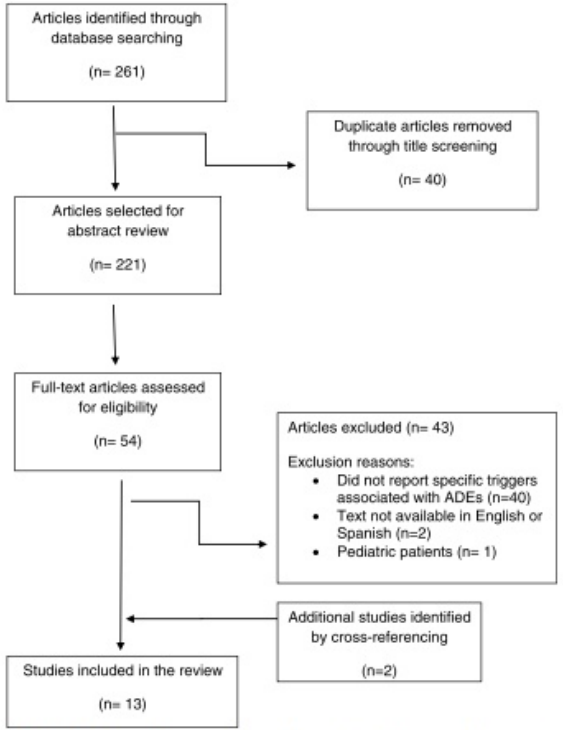
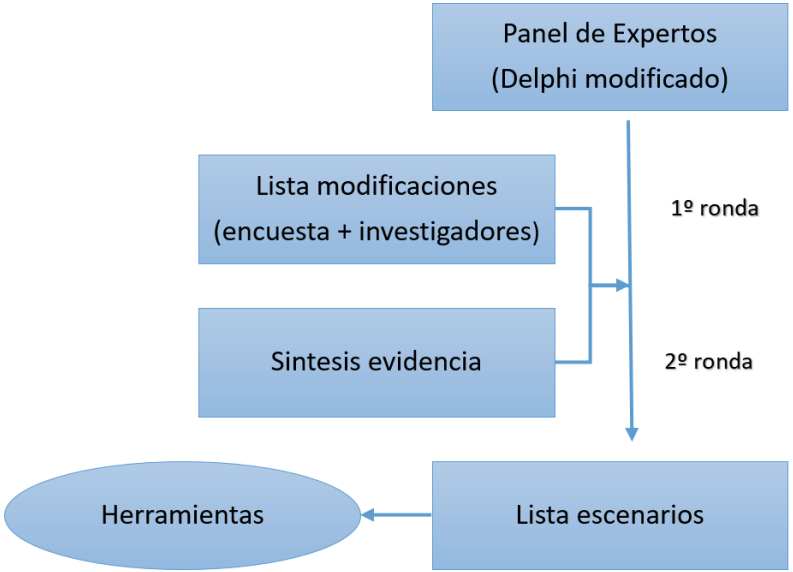


FIGURE 1. Flow diagram of the selection of articles on triggers used to detect ADEs in adult patients.

Delphi modificado



Panel de expertos (12):

Mujeres-hombres
Expertos en seguridad o en crónicos
Distintos ámbitos
Médicos y farmacéuticos
Distintas CCAA y países

Delphi modificado

Las **señales alertantes** se evaluaron según 3 items:

Para cada señal

Tres grados de adecuación:

- ADECUADA: mediana del grupo de 7-9.
- DUDOSA: mediana del grupo de 4-6.
- INADECUADA: mediana del grupo de 1-3.

Número de indicación	CAPITULO 2: Módulo de medicamentos Parte 2	Solidez de la evidencia que lo apoya	Utilidad en el paciente crónico con multimorbilidad	Factibilidad de su aplicación en la práctica clínica
		1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
24	Administración de loperamida			
25	Administración de enema			
26	Anticuerpos antidigoxina			
27	Glucagón			
28	Administración de 50 ml de glucosa al 50% + 10 UI de Insulina rápida			
29	Vancomicina oral			
30	Heparinas de bajo peso molecular y CLCr< 60ml/min			
	ón de haloperidol			
	ón de risperidona			

	DESACUERDO	ACUERDO
Tamaño grupo	Número de miembros que evalúan en cada extremo (1-3 y 7-9)	Número de miembros que evalúan fuera del tramo de 3 puntos que contiene la mediana (1-3; 4-6; 7-9)
8-9-10	≥ 3	≤ 2
11-12-13	≥ 4	≤ 3
14-15-16	≥ 5	≤ 4

Tasa de respuesta: 100%

Figura 20. Diagrama de flujo del proceso desarrollado para obtener el primer listado de señales alertantes

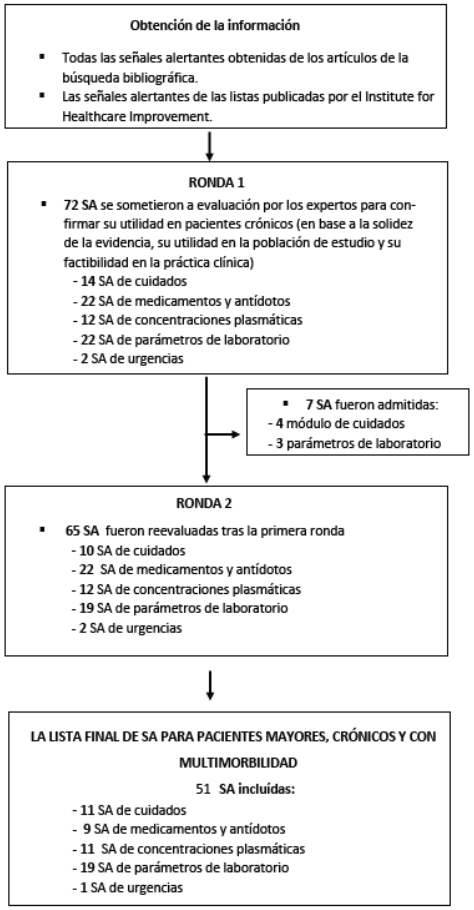


TABLE 2. Summary of the Results Obtained for the Scenarios Evaluated in the 2 Evaluation Rounds

Scenario	Triggers	Round 1 Result*	Round 2 Result†	Scenario	Triggers	Round 1 Result*	Round 2 Result†
Module 1. Care module triggers				41	Phenytoin >20 µg/mL	Re-evaluate	Included
1	Rash	Re-evaluate	Included	42	Phenobarbital > 45 µg/mL	Re-evaluate	Included
2	New allergy	Re-evaluate	Included	43	Valproic acid >120 µg/mL	Re-evaluate	
3	Oversedation/lethargy	Re-evaluate	Included	44	Gentamicin/Tobramycin levels: peak > 10 µg/mL, trough > 2 µg/mL	Re-evaluate	Included
4	Hypotension	Re-evaluate	Included				
5	Drop in systolic blood pressure	Re-evaluate	Excluded U				
6	Falls	Included	—	45	Amikacin levels: peak > 30 µg/mL, trough 10 µg/mL	Re-evaluate	Included
7	Transfusion or use of blood products	Included	—				
8	Diarrhea	Re-evaluate	Excluded UF	46	Vancomycin level: peak > 40 µg/mL and trough 20 µg/mL	Re-evaluate	Included
9	Constipation	Re-evaluate	Included				
10	Vomiting	Re-evaluate	Excluded F				
11	Acute dialysis	Re-evaluate	Included	47	Cyclosporine > 400 ng/L	Re-evaluate	Included
12	Unexpected medical or surgical emergency/sudden death	Re-evaluate	Included	48	Tacrolimus level >20 ng/mL	Re-evaluate	Included
				Module 4. Laboratory results module triggers			
13	Readmission within 30 d	Included	—	49	*Clostridium difficile*–positive stool	Re-evaluate	Included
14	Adverse reaction recorded	Included	—				
Module 2. Antidotes/treatments module triggers				50	Serum glucose < 50 mg/dL	Included	—
15	Vitamin K administration	Re-evaluate	Included	51	Serum glucose > 110 mg/dL	Re-evaluate	Included
16	Antihistamines IV	Re-evaluate	Included	52	Activated Partial Thromboplastin Time > 100 s	Re-evaluate	Excluded U
17	Prednisone and hydroxyzine	Re-evaluate	Excluded UF				
18	Flumazenil administration	Re-evaluate	Included				
19	Naloxone administration	Re-evaluate	Included	53	INR >5	Included	—
20	Methylnaltrexone	Re-evaluate	Excluded UF	54	Rising BUN or serum creatinine > 2 times baseline*	Re-evaluate	Included
21	Antiemetic administration	Re-evaluate	Included				
22	Ondansetron administration	Re-evaluate	Excluded U				
23	Antidiarrheals	Re-evaluate	Included U	55	eGFR <35 mL/min/1.73 m^2	Re-evaluate	Included
24	Loperamide administration	Re-evaluate	Included UF	56	K > 6.0 mEq/L	Re-evaluate	Included
25	Enema administration	Re-evaluate	Included UF	57	K < 2,9 mEq/L	Re-evaluate	Included
26	Digoxin immune fab	Re-evaluate	Included	58	Na < 130 mEq/L	Re-evaluate	Included
27	Glucagon	Re-evaluate	Excluded UF	59	Hypercalcemia > 10.5 mg/dL	Re-evaluate	Included
28	50 mL of dextrose 50% and 10 E Actrapid insulin administration	Re-evaluate	Excluded UF	60	ALT > 80 U/L and AST > 84 U/L	Re-evaluate	Included
				61	ALP > 350 U/L total bilirubin > 4 mg/dL	Re-evaluate	Included
29	Vancomycin oral	Re-evaluate	Excluded U				
30	Heparin low molecular weight and CL < 60 mL/h	Re-evaluate	Excluded F	62	CPK > 269 U/L	Re-evaluate	Included
				63	TSH < 0,34 µUI/L or T4 > 12 µg/dL	Re-evaluate	Included
31	Haloperidol administration	Re-evaluate	Included				
32	Risperidone administration	Re-evaluate	Included	64	TSH > 5,6 µUI/L or T4 < 6 µg/dL	Re-evaluate	Excluded U
33	Abrupt cessation of medication	Re-evaluate	Included				
34	Abrupt reduction of dose of medication	Re-evaluate	Excluded F	65	HA1C > 6% and glucocorticoid	Re-evaluate	Included
				66	WBC < 3.000	Re-evaluate	Included
35	Change of habitual medications	Re-evaluate	Excluded F	67	Platelet count < 50,000	Re-evaluate	Included
36	Long-term medications and	Re-evaluate	Included	68	Eosinophil > 9%	Re-evaluate	Excluded U
							Included
							-
							Excluded F
							Included

1. Módulo de SA de cuidados
2. Módulo de SA de medicamentos
3. Módulo de SA de concentraciones plasmáticas
4. Módulo de SA de parámetros analíticos
5. Módulo de SA de urgencias

Evaluación de la utilidad de las SA seleccionadas

ORIGINAL ARTICLE

Validating a Trigger Tool for Detecting Adverse Drug Events in Elderly Patients With Multimorbidity (TRIGGER-CHRON)

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Purpose: The aims of the study were to evaluate the performance of an initial list developed to detect adverse drug events (ADEs) in elderly patients with multimorbidity in clinical practice, to explore the possibility of shortening the list, and to use this tool to study the incidence and characteristics of the ADEs among this population.

Methods: This observational study was conducted at 12 Spanish hospitals. A random sample of five charts from each hospital was selected weekly for retrospective review for a 12-week period. We included patients aged 65 years and older with multimorbidity, hospitalized more than 48 hours. Adverse drug events were detected using a list of 51 triggers previously selected by an expert panel by means of a modified Delphi method. The number of triggers identified and ADEs detected were recorded. The severity and preventability of the ADEs were evaluated. The positive predictive value (PPV) of each trigger was calculated and used to select the most efficient triggers.

Results: In 720 charts reviewed, 1430 positive triggers were identified that led to detect 215 ADEs in 178 patients (24.7%), of which 13% were serious. One hundred nineteen ADEs (55.3%) were preventable and mainly related to inadequate treatment monitoring and prescribing errors. Triggers with a PPV of 5% or less were eliminated, resulting in a final list of 32 triggers (TRIGGER-CHRON) with a PPV of 22.1%, which accounted for 98.9% of all ADEs detected and 98.6% of the preventable ADEs.

Conclusions: The shorter final validated TRIGGER-CHRON tool is an efficient list for identifying ADEs in elderly patients with multimorbidity, detecting ADEs in one-fourth of hospitalized patients in internal medicine or geriatric units.

Key Words: chronic patient, drug-related adverse effects and adverse reactions/diagnosis, multimorbidity, patient safety

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systems across the world."[1] With this challenge, the WHO proposes to push forward and implement actions focused on improving medication safety and reducing the number of preventable adverse drug events (ADEs).

Polypharmacy is one of the key focus areas of this challenge. Currently, because of aging and increasing life expectancy, there are many more older patients who take multiple medications to treat more than one chronic disease. This intake has produced an increase in the likelihood of prescribing medication errors involving drug interactions, wrong dosages, etc, as well as patient-induced errors due to the difficulties inherent in keeping up with complex drug regimens.[2] Errors are also more frequent in the healthcare transitions, especially upon discharge from hospital to home.[3] The PRACtICe Study, carried out in the United Kingdom, designed to discover the nature of prescription errors in general practice during a 12-month period, found a rate of 30.1% of errors in patients who took five or more different drugs, a figure that increased along with the number of medications taken to a rate of 47% in patients who took 10 or more different drugs.[4] The number of drugs taken regularly is also the most frequently documented risk factor for serious ADEs, based on a systematic review of 26 studies including 85,212 patients.[5] It should be noted as well that older patients with multimorbidities are more likely to experience drug-related events and have higher ADE prevalence rates compared with other age groups.[6]

To make progress in improving medication safety and achieving the objective of reducing the number of errors for this challenge, health care organizations must have at their disposal an efficient, straightforward method to measure ADEs and to monitor the results of improvement interventions as they are implemented. Bearing in mind what has been stated previously, it would be very advantageous to have a special tool to detect ADEs

Estudio multicéntrico, observacional, retrospectivo, desarrollado en 12 hospitales nacionales y liderado por el Hospital Universitario Virgen del Rocío (HUVR), durante 12 semanas (2017). Revisión de HC

Pacientes crónicos con multimorbilidad
Edad > 65 años
Ingreso > 48 horas en MI o GRT

Evaluación de la utilidad de las SA seleccionadas

- ✓ Estudio piloto (2 semanas, CRDe)
- ✓ Los lunes: secuencia de aleatorización de los pacientes dados de alta la semana previa.
- ✓ Selección de los 5 primeros
- ✓ Criterios de inclusión/exclusión
- ✓ Se aplicaba la herramienta revisando la HC

- Gravedad: NCCMERP (se descartaron las categorías A y D, no daño)
- Evitabilidad: Cuestionario Schumock y Thornton adaptado por Otero et al.
  Si el EAM era evitable: Ruiz-Jarabo 2000 (clasificación tipo de error).
- Selección de los Trigger-Chron: Valor predictivo positivo > 5%: global, módulos, SA. Porcentaje de pacientes con resultado de SA positivo que sufre EAM entre el porcentaje de pacientes con esa SA.

Evaluación de la utilidad de las SA seleccionadas

Resultados:
720 pacientes; 55% mujeres; edad media 82,9 (DS 7,1)

1.430 SA (2 SA/pac)

215 EAM en 178 pac (24,7%)

EAM/ 100 PC: 29,9%

119 EAM evitables

Gravedad: la categoría mayoritaria fue la E (187/215; 87,0%)

GRAVEDAD		
E	87%	El error contribuyó o causó daño temporal al paciente y precisó intervención
F	12,1%	El paciente precisó o causó daño temporal y preciso o prolongó la hospitalización
G	0%	El error contribuyó o causó daño permanente al paciente
H	0,5%	El error comprometió la vida del paciente y se precisó intervención para mantenerlo con vida
I	0,5%	El error contribuyó o causó la muerte del paciente

TABLE 3. Frequency of Errors Associated With the 119 Preventable ADEs

	Error* (n = 119)	
Type of Medication Error	**n**	**(%)**
Inadequate therapy monitoring	38	(31.4)
Wrong dose	38	(31.4)
Drug/dose omission	23	(19.0)
Wrong/inappropriate drug	6	(5.0)
Wrong frequency	3	(2.5)
Other types	13	(10.7)
Total	121	

*In some preventable ADEs, more than 1 type of error could be present in 1 ADE.

TABLE 4A. Prevalence of Triggers and ADEs and PPV of Triggers

Triggers selected = TRIGGER-CHRON		No. Triggers Found in the Charts	Total ADEs* (n = 215)			Preventable ADEs* (n = 119)		
			n	(%)	PPV, %	n	(%)	PPV, %
Module 1. Care triggers		**391**	**113**	**(40.51)**	**28.9**	**59**	**(39.07)**	**15.01**
	Rash	11	2	(0.72)	18.2	1	(0.66)	9.1
	New allergy	3	1	(0.36)	33.3	1	(0.66)	33.3
R	Oversedation/lethargy	81	25	(8.96)	30.9	16	(10.6)	19.8
R	Hypotension	82	28	(10.04)	34.1	10	(6.62)	12.2
R	Transfusion or use of blood products	63	5	(1.79)	7.9	1	(0.66)	1.6
R	Constipation	100	25	(8.96)	25	18	(11.92)	18
R	Adverse reaction recorded	51	27	(9.68)	50	12	(7.95)	23.5
Module 2. Antidotes/treatments		**263**	**63**	**(22.59)**	**23.95**	**31**	**(20.52)**	**11.79**
R	Vitamin K administration	30	6	(2.15)	20	5	(3.31)	16.7
	Antihistamines IV	8	2	(0.72)	25	1	(0.66)	12.5
	Flumazenil administration	5	3	(1.08)	60	3	(1.99)	60
	Naloxone administration	4	2	(0.72)	50	2	(1.32)	50
R	Antiemetic administration	63	8	(2.87)	12.7	2	(1.32)	3.17
R	Haloperidol administration	84	5	(1.79)	5.9	4	(2.65)	4.8
R	Abrupt cessation of medication	69	37	(13.26)	53.6	14	(9.27)	20.3
Module 3. Medication concentration triggers		**9**	**3**	**(1.08)**	**33.33**	**3**	**(1.98)**	**33.33**
	Digoxin level > 2 ng/mL	8	2	(0.72)	25	2	(1.32)	25
	Carbamazepine >13 µg/mL	1	1	(0.36)	100	1	(0.66)	100
Module 4. Laboratory results triggers		**575**	**96**	**(34.43)**	**16.69**	**55**	**(36.41)**	**9.57**
	Clostridium difficile–positive stool	5	2	(0.72)	40	2	(1.32)	40
	Serum glucose <50 mg/dL	16	2	(0.72)	12.5	1	(0.66)	6.3
R	Serum glucose >110 mg/dL	182	38	(13.62)	25	23	(15.23)	12.7
R	INR > 5	25	8	(2.87)	32	8	(5.30)	32
	Rising BUN or serum creatinine > 2 times baseline*	11	1	(0.36)	9.1	0	(0)	0
R	e GFR < 35 mL/min/1.73 m^2	147	10	(3.58)	6.8	4	(2.65)	2.7
R	K > 6.0 mEq/L	26	7	(2.51)	26.9	6	(3.98)	23.1
R	K < 2,9 mEq/L	30	9	(3.23)	30	4	(2.65)	13.3
R	Na < 130 mEq/L	55	7	(2.51)	12.7	2	(1.32)	3.6
	ALT >80 U/L and AST > 84 U/L	24	3	(1.08)	12.5	1	(0.66)	4.2
	ALP > 350 U/L total bilirubin >4 mg/dL	8	1	(0.36)	12.5	0	(0)	0
	CPK > 269 U/L	16	1	(0.36)	6.3	1	(0.66)	6.3
	TSH < 0.34 µUI/L or T4 > 12 µg/dL	7	1	(0.36)	14.3	1	(0.66)	14.3
R	HA1C > 6% and glucocorticoid	7	5	(1.79)	71.4	2	(1.32)	28.6
	White blood cell <3000	16	1	(0.36)	6.3	0	(0)	0
Module 5. Emergency department triggers		**9**	**1**	**(0.36)**	**11.1**	**1**	**(0.66)**	**11.1**
	Readmission to ED within 48 hours	9	1	(0.36)	11.1	1	(0.66)	11.1
Performance of the 16 "R" triggers (Reduced TRIGGER-CHRON)		1095	250	(89.61)	22.83	131	(86.75)	11.96
Subtotal of triggers selected		1247	276	(98.92)	22.13	149	(98.64)	11.95

Triggers included in TRIGGER-CHRON and in the reduced TRIGGER-CHRON.

TABLE 4B. Prevalence of Triggers and ADEs and PPV of Triggers

Triggers Not Selected	No. Triggers Found in the Charts	Total ADEs* (n = 215)			Preventable ADEs* (n = 119)		
		n	(%)	PPV, %	n	(%)	PPV, %
Module 1. Care triggers	**60**	**1**	**(0.36)**	**1.67**	**1**	**(0.36)**	**1.67**
Falls	6	0	(0)	0	0	(0)	0
Acute dialysis	1	0	(0)	0	0	(0)	0
Unexpected medical or surgical emergency/sudden death	5	0	(0)	0	0	(0)	0
Readmission within 30 d	48	1	(0.36)	2.1	1	(0.66)	0.36
Module 2. Antidotes/treatments triggers	**82**	**1**	**(0.36)**	**1.22**	**1**	**(0.66)**	**1.22**
Risperidone administration	36	1	(0.36)	2.8	1	(0.66)	0.36
Long-term medications and classifications are at variance	46	0	(0)	0	0	(0)	0
Module 3. Medication concentration triggers	**3**	**0**	**(0)**	**0**	**0**	**(0)**	**0**
Lithium >1.5 mmol/L	0	0	(0)	NA	0	(0)	NA
Phenytoin >20 µg/mL	0	0	(0)	NA	0	(0)	NA
Phenobarbital >45 µg/mL	0	0	(0)	NA	0	(0)	NA
Valproic acid >120 µg/mL	0	0	(0)	NA	0	(0)	NA
Gentamicin/tobramycin levels: peak >10 µg/mL, trough >2 µg/mL	0	0	(0)	NA	0	(0)	NA
Amikacin levels: peak >30 µg/mL, trough 10 µg/mL	0	0	(0)	NA	0	(0)	NA
Vancomycin level: peak >40 µg/mL and trough 20 µg/mL	3	0	(0)	0	0	(0)	0
Cyclosporine >400 ng/L	0	0	(0)	NA	0	(0)	NA
Tacrolimus level > 20 ng/mL	0	0	(0)	NA	0	(0)	NA
Module 4. Laboratory results triggers	**38**	**1**	**(0.36)**	**2.63**	**0**	**(0)**	**0**
Hypercalcemia >10.5 mg/dL	2	0	(0)	0	0	(0)	0
Platelet count <50,000	5	0	(0)	0	0	(0)	0
Hemoglobin >12 g/dL	2	0	(0)	0	0	(0)	0
Decrease in hemoglobin or hematocrit > 25%	29	1	(0.36)	3.5	0	(0)	0
Subtotal triggers not selected	183	3	(1.08)	1.6	2	(1.32)	1.1
Total of all triggers	1430	279	(100)	19.5	151	(100)	10.6

Triggers not included in TRIGGER-CHRON

Evaluación de la utilidad de las SA seleccionadas

TRIGGER -CHRON

Estas 32 SA representaron el 98,9% de todos los EAM y el 98,6% de los EAM evitables

SEÑALES ALERTANTES	VPP (%)
Módulo 1. Cuidados	**28,9**
Rash	18,2
Nueva alergia	33,3
Letargia o sobresedación	30,9
Hipotensión	34,1
Trasfusión o uso de hemoderivados	7,9
Estreñimiento	25
Reacción adversa registrada	50
Módulo 2. Medicamentos y antídotos	**23,9**
Administración de vitamina K	20
Uso de antihistamínicos intravenosos	25
Uso de flumazenilo	60
Uso de naloxona	50
Uso de antieméticos	12,7
Uso de haloperidol	5,9
Suspensión brusca de la medicación	53,6
Módulo 3. Concentraciones plasmáticas	**33,3**
Digoxina > 2 ng/Ml	25
Carbamazepina > 12 µg/mL	100

SEÑALES ALERTANTES	VPP (%)
Módulo 4. Parámetros analíticos	**16,7**
Toxina de C. difficile positiva en heces	40
Glucosa < 50 mg/Dl	12,5
Glucemia > 110 mg/dL	25
INR > 5	32
Aumento del BUN o Cr mayor de dos veces los niveles basales*	9,1
CL Cr < 35 ml/min/1,73m2	6,8
K > 6,0 mEq/L	26,9
K < 2,9 mEq/L	30
Na < 130 mEq/L	12,7
ALT > 80 U/L and AST > 84 U/L	12,5
FA > 350 U/L bilirrubina total > 4 mg/dL	12,5
CPK > 269 U/L	6,3
TSH < 0,34 µUI/L ó T4>12 µg/dL	14,3
HA1c > 6% y glucocorticoides	71,4
Leucocitos < 3000/ mm3	6,3
Módulo 5. Urgencias	**11,1**
Reingreso en urgencias en menos de 48 h.	11,1
Subtotal de las SA seleccionadas	**22,1**

16 SA: detectan el 89,6% de todos los EAM y el 86,8% de los EAM evitables

Tabla 28. Resultados del TRIGGER-CHRON reducido

SEÑALES ALERTANTES		Nº de SA encontradas	Total EAM[a]			EAM evitables[a]		
			N	%	VPP (%)	n	%	VPP (%)
SA seleccionadas = TRIGGER CHRON								
R	Letargia o sobresedación	81	25	8,9	30,9	16	10,6	19,8
R	Hipotensión	82	28	10,0	34,1	10	6,6	12,2
R	Trasfusión o uso de hemoderivados	63	5	1,8	7,9	1	0,7	1,6
R	Estreñimiento	100	25	8,9	25	18	11,9	18
R	Reacción adversa registrada	51	27	9,7	50	12	7,9	23,5
R	Administración de vitamina K	30	6	2,1	20	5	3,3	16,7
R	Uso de antieméticos	63	8	2,9	12,7	2	1,3	3,2
R	Uso de haloperidol	84	5	1,8	5,9	4	2,6	4,8
R	Suspensión brusca de la medicación	69	37	13,3	53,6	14	9,3	20,3
R	Glucemia > 110 mg/dL	182	38	13,6	25	23	15,2	12,7
R	INR > 5	25	8	2,9	32	8	5,3	32
R	CL Cr < 35 ml/min/1,73m^2	147	10	3,6	6,8	4	2,6	2,7
R	K > 6,0 mEq/L	26	7	2,5	26,9	6	3,9	23,1
R	K < 2,9 mEq/L	30	9	3,2	30	4	2,6	13,3
R	Na < 130 mEq/L	55	7	2,5	12,7	2	1,3	3,6
R	HA1c > 6% y glucocorticoides	7	5	1,8	71,4	2	1,3	28,6
Utilidad de 16 señales alertantes (TRIGGER-CHRON reducido)		1095	250	89,6	22,8	131	86,7	12,0

Cl Cr: aclaramiento de creatinina; INR: índice internacional normalizado; R: SA incluidas en la herramienta reducida.

[a] En ocasiones un EAM podía ser identificado con más de una SA

Selección de las SA más eficientes para detectar EAM incluidos en la lista MARC

Original research

Utility of a trigger tool (TRIGGER-CHRON) to detect adverse events associated with high-alert medications in patients with multimorbidity

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ABSTRACT

Objective To determine the utility of a tool (TRIGGER-CHRON) for identifying adverse drug events (ADEs) associated with the administration of high-alert medications in elderly patients with multimorbidity and to determine the medications most frequently implicated.

Methods A retrospective observational study was conducted at 12 Spanish hospitals. A random sample of five medical records from each hospital was selected weekly for review over a 12-week period. We included patients aged 65 and over with multimorbidities, hospitalised for >48 hours. ADEs detected by the 32 TRIGGER-CHRON signals and caused by high-alert medications included on the Spanish HAMC list for chronic patients were selected for analysis. Triggers identified and ADEs detected were recorded. The severity and preventability of the ADEs were evaluated. The positive predictive value (PPV) of each trigger was calculated.

Results On 720 charts reviewed, 908 positive triggers were identified that led to the detection of 158 ADEs caused by at least one high-alert medication on the HAMC list. These ADEs occurred in 139 patients (prevalence 19.3/100 admissions). The majority of ADEs were mild and 59.5% were deemed preventable. The drugs most frequently associated with ADEs were corticosteroids, loop diuretics, opioid analgesics and oral

Recognising this problem, the WHO launched its third Global Patient Safety Challenge: Medication Without Harm in March 2017, with the goal of reducing severe avoidable medication-related harm by 50% over the next 5 years, globally.[2] The WHO has asked countries and key stakeholders to prioritise three areas that are associated with high medication error rates for early actions: transitions of care, inappropriate polypharmacy and high-risk situations, which includes the use of high-alert medications.[3]

The concept of 'high-alert or high-risk medications', referring to those medications that bear a heightened risk of causing significant patient harm when used in error, is a key concept in patient safety. The Institute for Safe Medication Practices (ISMP) introduced this concept in 1998 after conducting a study which revealed that a relatively small number of medications was responsible for the majority of medication errors resulting in serious consequences for patients.[4] Hence, it was proposed that efforts should focus on improving the safe use of these medications to make them more efficient and to avoid preventable harm to patients.[5] Specific medications considered high-alert drugs may differ because the medications most likely associated with harm vary depending on the setting and disease

Table 1 List of triggers included in the TRIGGER-CHRON and high-alert medications whose potential adverse drug events could be detected using these triggers

TRIGGER-CHRON		High-alert medications
Module 1: Care triggers		
C1	Rash	All medications
C2	New allergy	All medications
C3	Oversedation/lethargy	Antipsychotics, benzodiazepines, opioids
C4	Hypotension	β-adrenergic blockers, loop diuretics, spironolactone/eplerenone
C5	Transfusion or use of blood products	Oral anticoagulants, antiplatelets, NSAIDs
C6	Constipation	Opioids
C7	Adverse reaction recorded	All medications
Module 2: Antidotes/drug treatments		
D1	Vitamin K administration	Oral anticoagulants
D2	Antihistamines IV	All medications
D3	Flumazenil administration	Benzodiazepines
D4	Naloxone administration	Opioids
D5	Antiemetic administration	Cytostatic drugs, opioids, others
D6	Haloperidol administration	Opioids
D7	Abrupt cessation of medication	All medications
Module 3: Medication plasma concentration triggers		
P1	Digoxin level >2 ng/mL	Digoxin
P2	Carbamazepine >12 µg/mL	Antiepileptics
Module 4: Laboratory results triggers		
L1	*Clostridium difficile* positive stool	–
L2	Serum glucose <50 mg/dL	Insulins, oral hypoglycaemic drugs
L3	Serum glucose >110 mg/dL	Corticosteroids, insulins
L4	INR >5	Oral anticoagulants
L5	Rising BUN or serum creatinine >2 times baseline	Loop diuretics, NSAIDs, amiodarone/dronedarone, spironolactone/eplerenone
L6	eGFR <35 mL/min/1.73m^2	Loop diuretics, immunosuppressants, NSAIDs, spironolactone/eplerenone
L7	K >6.0 mEq/L	Immunosuppressants, loop diuretics, spironolactone/eplerenone
L8	K <2.9 mEq/L	Loop diuretics
L9	Na <130 mEq/L	Loop diuretics, spironolactone/eplerenone
L10	ALT >80 U/L and AST >84 U/L	Cytostatic drugs, corticosteroids
L11	ALP >350 U/L and total bilirubin >4 mg/dL	Cytostatic drugs, corticosteroids
L12	CPK >269 U/L	Cytostatic drugs
L13	TSH <0.34 µUI/L or T4 >12 µg/dL	Amiodarone/dronedarone, cytostatic drugs
L14	HbA1c >6% and glucocorticoid	Corticosteroids
L15	White blood cells <3000	Cytostatic drugs, immunosuppressants, methotrexate
Module 5. Emergency department (ED) triggers		
E1	Readmission to ED within 48 hours	All medications

ALP, alkaline phosphatase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; CPK, creatine phosphokinase; GFR, glomerular filtration rate; HbA1c, glycated haemoglobin; INR, International normalised ratio; NSAIDs, non-steroidal anti-inflammatory drugs; TSH, thyroid-stimulating hormone.

Se incluyeron 32 SA relacionadas con los medicamentos de la lista MARC

Resultados:

215 EAM: 158 relacionados con los MARC (74,5%); 139 pacientes (58% mujeres; edad media 83,7)

Prevalencia de EAM detectados con los Trigger-Chron de la lista MARC: 19,3 / 100 ingresos (casi el 20%)

94 EAM fueron potencialmente prevenibles (59,5%; 94/158)

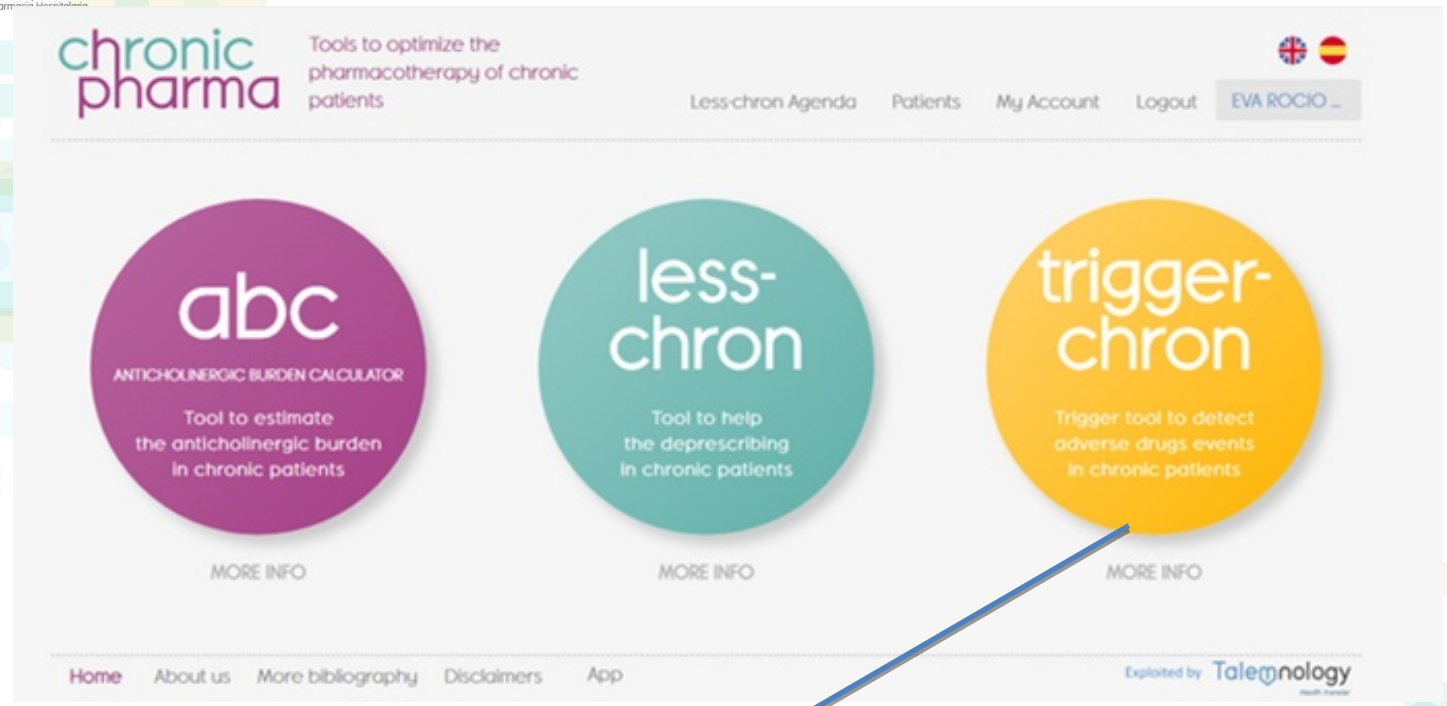
EAM detectados incluidos en la lista MARC, gravedad y evitabilidad

Medicamentos incluidos en la lista MARC	EAM detectados* n= 158 (%)	Gravedad				Evitabilidad	
		E	F	G	H	SI n=94 (59,5%)	No n= 64 (40,5%)
Corticosteroides	38 (24,1%)	37	1	-	-	21	17
Diuréticos del asa	30 (19,0%)	27	3	-	-	15	15
Opioides	26 (16,5%)	23	2	1	-	21	5
Anticoagulantes orales	21 (13,3%)	15	6	-	-	16	5
Antipsicóticos	14 (8,9%)	13	1	-	-	9	5
Espironolactona/ eplerenona	9 (5,7%)	9	-	-	-	3	6
Antiagregantes plaquetarios (incluyendo la aspirina)	7 (4,4%)	3	4	-	-	2	5
Benzodiacepinas y análogos	7 (4,4%)	7	-	-	-	7	-
Insulinas	5 (3,2%)	3	1	-	1	3	2
B-bloqueantes adrenérgicos	3 (1,9%)	3	-	-	-	-	3
Hipoglucemiantes orales	2 (1,3%)	-	2	-	-	1	1
Digoxina	2 (1,3%)	2	-	-	-	2	-
Antiepilépticos de estrecho margen terapéutico	1 (0,6%)	1	-	-	-	1	-
Antiinflamatorios no esteroideos	1 (0,6%)	1	-	-	-	-	1
Inmunosupresores	1 (0,6%)	-	1	-	-	1	-
Total	167	144	21	1	1	102	65

Prevalencia de EAM y VPP de cada SA:

25 SA de las 32 del Trigger-Chron detectaron EAM causados por medicamentos incluidos en la lista MARC, VPP>6%.

Señal alertante (TRIGGER-CHRON)	Nº de EAM detectados con la SA *	Nº de activaciones de la SA en las HC	VPP (%)	Medicamento de la lista MARC implicado en el EAM (n) ∓
Glucemia > 110 mg/dL	38	182	20,9	Corticosteroides (36), Insulinas (2)
Suspensión brusca de la medicación	32	60	53,3	ACO (8), diuréticos del asa (7), Antiagregantes plaquetarios (5), Antipsicóticos (4), Benzodiacepinas (3), β-bloqueantes (2), Espironolactona (2), Insulinas (1)
Letargia o sobresedación	22	71	30,9	Antipsicóticos (13), Benzodiacepinas (5), Opioides (4)
Hipotensión	19	56	33,9	Diuréticos del asa (15), β-bloqueantes (3), Espironolactona (1)
Reacción adversa registrada	19	38	50	ACO (5), Diuréticos del asa (3), Opioides (3), Benzodiacepinas (2), Hipoglucemiantes orales (2), Espironolactona (2), Antiagregantes plaquetarios (1), AINEs (1)
Estreñimiento	18	72	25	Opioides (18)
INR > 5	8	25	32	ACO (8)
CL Cr < 35 ml/min/1,73m^2	7	99	7,1	Diuréticos del asa (4), Espironolactona (2), Inmunosupresores (1)
Administración de vitamina K	6	30	20	ACO (6)
K < 2,9 mEq/L	6	20	30	Diuréticos del asa (6)
Trasfusión o uso de hemoderivados	5	63	7,9	Antiagregantes plaquetarios (3), ACO (2)
K > 6,0 mEq/L	5	18	27,7	Diuréticos del asa (3), Espironolactona (2)
HA1c > 6% y glucocorticoides	5	7	71,4	Corticosteroides (5)
Uso de antieméticos	4	31	12,9	Opioides (3), Digoxina (1)
Uso de flumazenilo	3	5	60	Benzodiacepinas (3)
Uso de haloperidol	3	50	6	Antipsicóticos (2) Opioides (1)
Glucosa < 50 mg/dl	2	16	12,5	Insulinas (2)
Uso de naloxone	2	4	50	Opioides (2)
Digoxina > 2 ng/mL	2	8	25	Digoxina (2)
Carbamazepina > 12 µg/mL	1	1	100	Antiepilépticos (1)
Aumento del BUN o Cr mayor de dos veces los niveles basales	1	11	9,1	Diuréticos del asa (1)
Na < 130 mEq/L	1	8	12,5	Espironolactona (1)
ALT > 80 U/L y AST > 84 U/L	1	8	12,5	Corticosteroides (1)
CPK > 269 U/L	1	16	6,3	Corticosteroides (1)
Reingreso en urgencias en menos de 48 horas	1	9	11,1	Diuréticos del asa (1)
Total	212	908		



Herramienta con 32 SA para detectar EAM en pacientes mayores con multimorbilidad

A CORUÑA
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