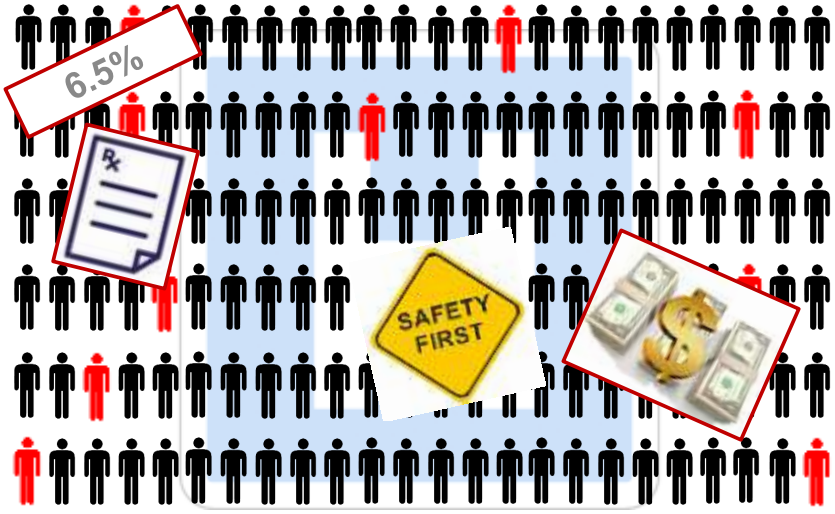
Detection of drug related problems by automated screening of patients' electronic medical records: useful or harmful to the clinical pharmacist?"

Vera Jordan-von Gunten

48th ESCP Symposium on Clinical Pharmacy
Ljubljana, October 24, 2019

Context in hospitals

Adverse drug events



Forster AJ. J Am Med Inform Assoc. 2012; Lazarou J. JAMA. 1998; Classen DC, JAMA. 1997; Howard RL. Qual Saf Health Care. 2003; Formica D. Expert Opin Drug Saf. 2018:

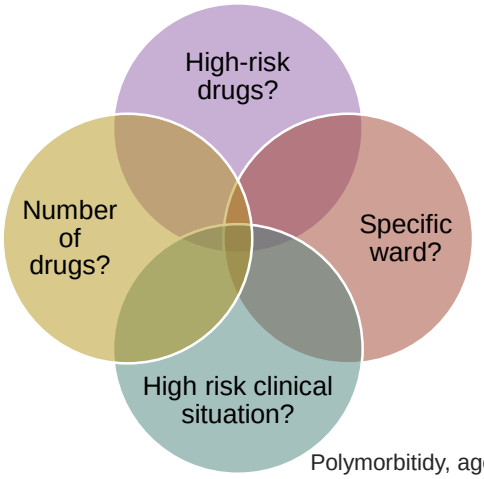
How can we assess that drug are used safely?

- Pharmacist has proven his role in identification and prevention of Drug Related Problems
- Improved medication use and patient outcome

- ↑ Nb of prescriptions,
- ↑ Nb of patients,
- ↑ Complexity of patients,
- Multimorbidity/Polypharmacy
- Limited resources

PRIORITIZATION TOOLS
TARGETING THE RIGHT PATIENTS

Who are the right patients?



Polymorbitidy, age, disability, organ failure?

Patient prioritization


Editorial

Lewis P. Eur J Hosp Pharm 2017;**24**:314.

Research in Social and Administrative Pharmacy

Volume 15, Issue 6, June 2019, Pages 767-779

Patient prioritization for pharmaceutical care in hospital: A systematic review of assessment tools

Meshal A. Alshakrah, Douglas T. Steinke, Penny J. Lewis

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https://doi.org/10.1016/j.sapharm.2018.09.009

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Patient prioritization : tools

- 19 studies evaluating 17 tools for assessing the risk of DRPs and prioritizing patients at the greatest risk of DRPs
- Published over the last 6 years
- Mostly from the UK and Europe
- 10/17 tools are electronic tools (references)

Alshakrah MA, *Research in Social & Administrative Pharmacy* (2018), doi: https://doi.org/10.1016/j.sapharm.2018.09.009.

Patient prioritization : thematic analysis

- Impact of the tool on patient care
- Impact of the tool on delivery of pharmacy services
- Tool limitations (incompleteness)
- Identified risk factors

Alshakrah MA, Steinke DT, Lewis PJ, Patient prioritization for pharmaceutical care in hospital: A systematic review of assessment tools, *Research in Social & Administrative Pharmacy* (2018), doi: https://doi.org/10.1016/j.sapharm.2018.09.009.

Patient prioritization : risk factors included

19 studies evaluating 17 tools

Risk factors (patient related) :
- Age
- Renal impairment
- Comorbidity

High risk drug classes:
- Anticoagulants
- Cardiovascular
- Antiepileptic drugs
- Antimicrobials
- Chemotherapy
- Immunosuppressants
- Insulin
- Opiates

Risk factors (drug related) :
- High risk medication
- Drugs requiring monitoring
- Polypharmacy

Alshakrah MA, Steinke DT, Lewis PJ, Patient prioritization for pharmaceutical care in hospital: A systematic review of assessment tools, *Research in Social & Administrative Pharmacy* (2018), doi: https://doi.org/10.1016/j.sapharm.2018.09.009.

Patient prioritization tool : ART

- Development of an electronic patient tool to help prioritizing inpatients for interventions to prevent ADE

- **Assessment of risk tool (ART) → 38 flags (in 5 groups)**
  - Patient profile (e.g. age, race, comprehension difficulties, compliance)
  - Patient encounter (e.g. frequent admissions, ICU, mental health…)
  - Clinical profile – chronic diseases (e.g. enrolment in COPD / diabetes programs…)
  - High-risk medication (e.g. polypharmacy, antiepileptics, anticoagulants…)
  - Laboratory values (e.g. renal function, potassium, glycemia…)

Falconer et al. Development of an electronic patient prioritization tool for clinical pharmacist interventions. Am J Health Syst Pharm. 2014 Feb 15;71(4):311-20
Falconer et al., Validation of the assessment of risk tool: patient prioritisation technology for clinical pharmacist interventions Eur J Hosp Pharm 2017;0:1–7.

Patient prioritization tool : ART

Table 3.
ART Flag Group 3 (Clinical Profile—Patients With Chronic Disease)[a]

No.	Description	Flag[b]	Score

Table 5.
ART Flag Group 5 (Laboratory Values)[a]

No.	Description	Flag[b]	Score
1	Admitted patients with one of the following test results: eGFR of <30 mL/min/1.73 m² in past 5 days, SCr >200 µmol/L (>2.2 mg/dL) in past 5 days	Poor Renal Function	8
2	All currently admitted patients with one of the following test results: WBC count of <3 × 10⁹/L (<3 × 10³/mm³) in past 5 days, neutrophil count of <1.5 × 10⁹/L (<1.5 × 10³/mm³) in past 5 days	Infection Risk (WBC)	4
3	All currently admitted patients with one of the following test results: INR of >3.5 in past 5 days, aPTT of >100 sec in past 5 days	Coagulation Risk	10
4	All currently admitted patients with potassium concentration of <3 or >6 mmol/L (<3 or >6 meq/L) in past 5 days	Potassium	10

	identified via medication reconciliation process within previous 12 mo		
2	Admitted patients receiving 1 or more antiepileptic medications from Pyxis® during current admission	Antiepileptic Meds	2

→ provide early interventions for patients with greatest need
→ Updated during hospital stay
→ Clinical Rx's positive feed-back

Complexity score based on preventable ADEs

- **Aim**: development of an electronic complexity-score (C-score) that ranks hospitalized patients for clinical intervention, according to their risk for pADEs.
- List of pADEs assembled through literature review
- Ranked by ASHP members and expert panel (overall importance, prevalence, severity, preventability, measurability) → risk models
- Defined risk populations for each specific pADE
- Measured the incidence of the pADE in the specific risk population
- Other variables included in the prediction model to develop the C-score

Jeon N, et al.. Identifying and characterizing preventable adverse drug events for prioritizing pharmacist intervention in hospitals. Am J Health Syst Pharm. 2017 Nov 1;74(21):1774-1783.
Jeon N, et al.. Measurement of selected preventable adverse drug events in electronic health records: Toward developing a complexity score. Am J Health Syst Pharm. 2017 Nov 15;74(22):1865-1877.
Winterstein AG, et al. Development and validation of a complexity score to rank hospitalized patients at risk for preventable adverse drug events. Am J Health Syst Pharm. 2017 Dec 1;74(23):1970-1984.

Complexity score based on preventable ADEs

pADE
Uncontrolled postsurgical pain
Uncontrolled pneumonia[a]
Drug-associated hypotension
Uncontrolled *Clostridium difficile* infection[a]
Uncontrolled hypertension
Uncontrolled hyperglycemia
Drug-associated hypoglycemia
Hypokalemia
Drug-associated QT interval prolongation[a]
Hyponatremia
Drug-associated acute kidney injury[a]
Hyperkalemia
Drug-associated acute liver injury[a]
Drug-associated falls
Drug-associated acute mental status changes
Venous thromboembolism[a]

Jeon N, et al.. Measurement of selected preventable adverse drug events in electronic health records: Toward developing a complexity score. Am J Health Syst Pharm. 2017 Nov 15;74(22):1865-1877.

"Check of Medication Appropriateness"

- University Hospitals Leuven
- CPOE system integrated with a CDSS at prescription (DDI, drug food interaction, Pregnancy&Lactation)
- Identification of high-risk prescriptions generated by 78 advanced clinical rules integrating patient specific characteristics, grouped in 5 therapeutic categories
- Back office clinical service : worklist with alerts aiming at hospital pharmacists → evaluation by clinical pharmacist
- → note in patient medical record, or contact physician by phone (critical situations)

Quintens et al. Development and implementation of "Check of Medication Appropriateness" (CMA): advanced pharmacotherapy-related clinical rules to support medication Surveillance. BMC Medical Informatics and Decision Making; (2019) 19:29

"Check of Medication Appropriateness"

Table 1 Pharmacotherapeutic categories and subcategories used to define the clinical rules[4]

	Category (and subcategories)	Example of a clinical rule
1	Overrules of alerts for very severe DDIs generated by the CDSS	Reduced effect of valproic acid by carbapenems leading to an increased risk of convulsions
2	Drugs with a restricted indication or dosing	Patient with high dose meropenem
3	Medication use potentially leading to biochemical changes	
	* *Drug use in renal insufficiency*	Patient with a CrCl < 30 ml/min and treated with metformin
	* *Drugs with high potential of QTc interval prolongation*	Patient with a QTc > 450/470 ms and treated with haloperidol
	* *Drug use associated with hyperpotassemia*	Patient with a K > 5.5 mmol/L and treated with an ACE inhibitor
	* *Drug use associated with hypopotassemia*	Patient with a K < 3.5 mmol/L and treated with flucloxacillin without potassium supplementation
	* *Drug use associated with supratherapeutic INR*	Patient with a supratherapeutic INR (INR > 4) and treated with a VKA
	* *Drug use associated with bone marrow suppression*	Patient with an absolute neutrophil count < $1.5*10^9$/L and treated with clozapine
4	Potential sequential therapy for bio-equivalent drugs	Potential sequential therapy for levofloxacine
5	Others	through enteral

- 8% of the alerts considered clinically relevant
- Acceptance level 56% when only a note was sent, 83% by phone

Quintens … A): advanced pharmac… tics and Decision …

A few ideas from other countries

Identify high risk drugs by analyzing most frequent pharmacists interventions (Digoxine, Colchicine, MTX, Oral anticoagulants)[1]

Include criteria about "Organizations at risk" = institutions where the LOS is > the national mean or patients coming through ER[3]

Assigning patients a "Patient Acuity Level" to prioritize the frequency of patient reviews and the seniority of pharmacists performing patient reviews[2]

Detect and prevent drug induced delirium through an algorithm combining anticholinergic burden scales and other risk factors[4]

[1]Mouterde AL, Bourdelin M, Maison O, Coursier S, Bontemps H. [Targeting high-risk drugs to optimize clinical pharmacists' intervention]. Therapie. 2016 Dec;71(6):595-603.

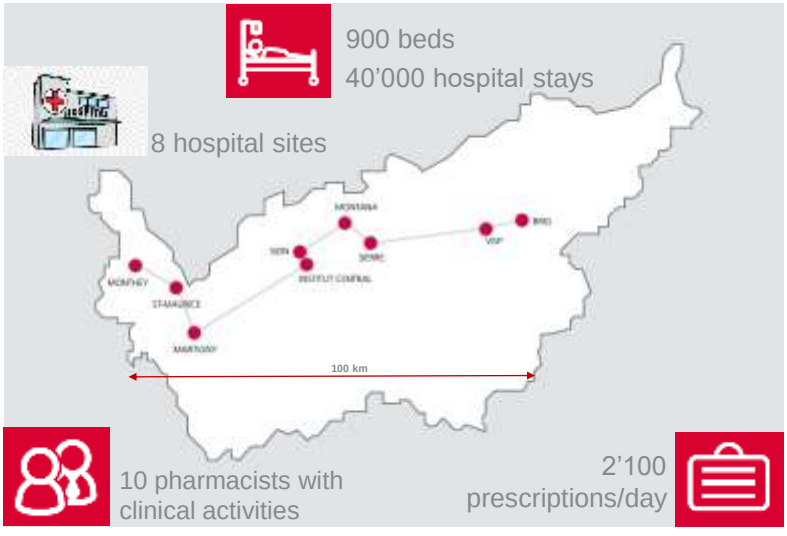
[2]Hickson RP, et al. Evaluation of a pharmaceutical assessment screening tool to measure patient acuity and prioritise pharmaceutical care in a UK hospital. Eur J Hosp Pharm 2017;**24**:74–79, doi:10.1136/ejhpharm-2015-000829

[3]Bigot A., Comment prioriser les activités de pharmacie clinique dans les unités de soins ? Elaboration d'un outil d'aide à la décision basé sur une analyse globale des risques. Thèse de doctorat, Toulouse 2015

[4]Lisibach A, Lutters M. Detection and prevention of delirium triggered by adverse drug events (DELIKT project), Hospital Baden (Switzerland), running.

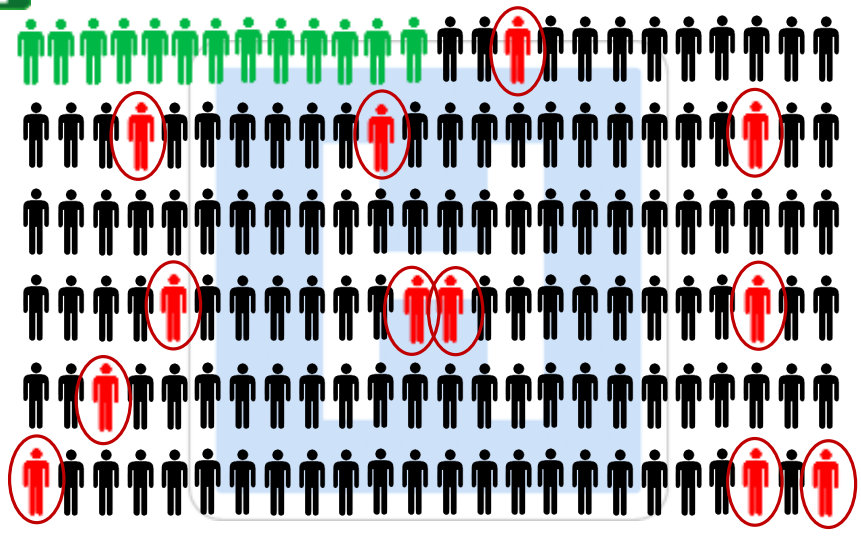
Hopital du Valais

Hopital du Valais (HVS)



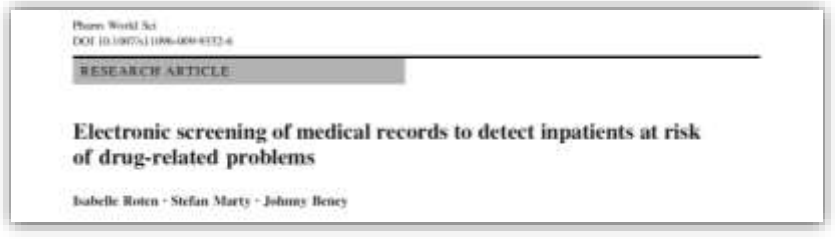
High risk patients…

… and pharmacy staffing



1st screening tool 2008

- In 2008, 1st version of the electronic screening tool in our pharmacy
- Screening with 6 algorithms (ATC Codes ± lab values)
- Aim: gain time to prepare clinical rounds
- Sensitivity 85%, Specificity 60.4%
- Too complicated to run on a daily basis


Pharm World Sci
DOI 10.1007/s11096-009-9372-6

RESEARCH ARTICLE

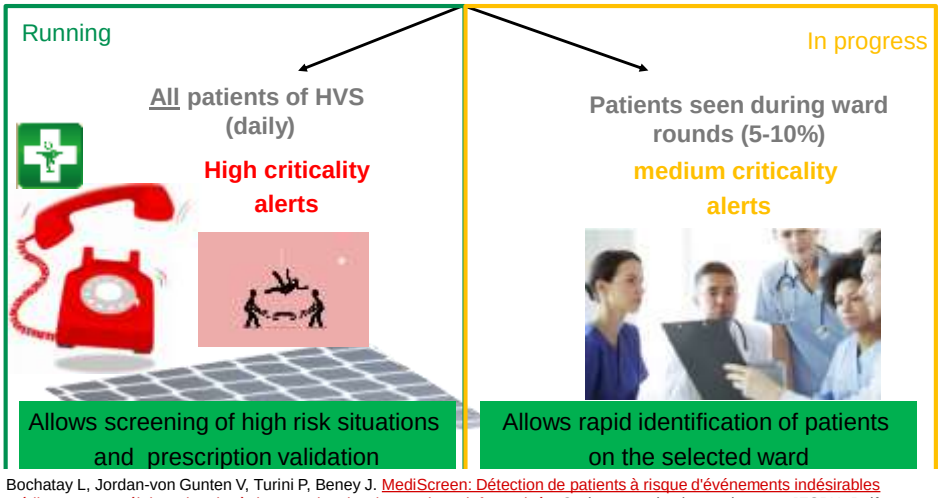
Electronic screening of medical records to detect inpatients at risk of drug-related problems

Isabelle Roten · Stefan Marty · Johnny Beney

Roten I(1), Marty S, Beney J. Electronic screening of medical records to detect inpatients at risk of drug-related problems. Pharm World Sci. 2010 Feb;32(1):103-7.

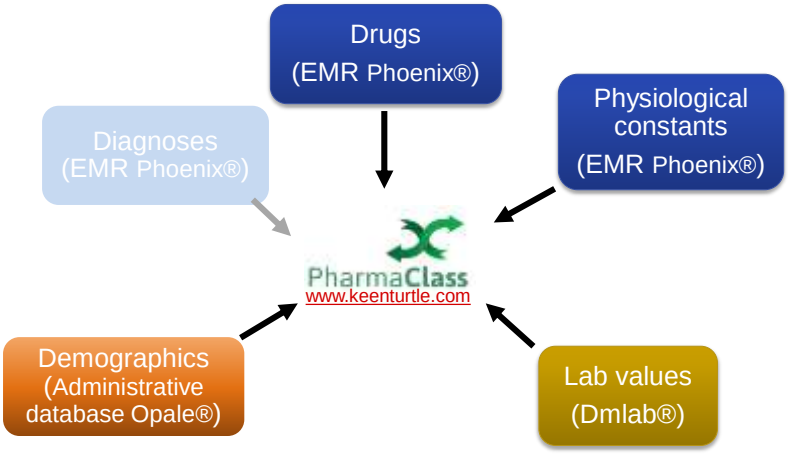
2nd screening tool (2018)

Aim of the project

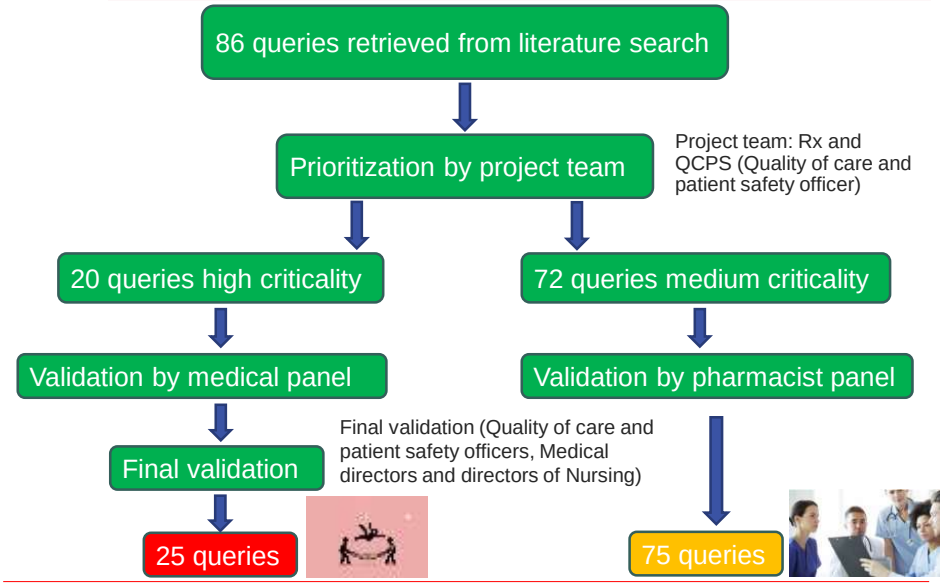


Bochatay L, Jordan-von Gunten V, Turini P, Beney J. MediScreen: Détection de patients à risque d'événements indésirables médicamenteux: élaboration de règles pour les dossiers patients informatisés; Oral communication and poster, JFSPH, Belfort, mars 2018. https://www.hopitalvs.ch/fr/professionnels-de-la-sante/institut-central-des-hopitaux/pharmacie/documentation.html

… Data from the EMR



Prioritization and validation of queries



Different types of alerts

Potential DRP → need to validate if DRP clinically relevant

Combination of 2 oral anticoagulants
Combination of azathioprine/mercato
Combination of clozapine and carba
Digoxin and K+ out of range
Digoxin and Digoxin-level > range
Vancomycin and Vancomycin-level <

Altered renal function (eGFR depending on drug) with:
- Colchicine
- Levetiracetam
- Methotrexate

hibitor
hibitor

Check-list for Vancomycin and level :
- Check pre-analytical aspects (timing of level)
- Check renal function
- If necessary, suggest new vancomycin dose regimen

Different types of alerts

High-risk drugs → need to check several parameters in medical record that cannot be extracted electronically

Presence of the following drug:
- Colchicine
- Methotre
- Drugs ca
- Immunos
- Mysoline

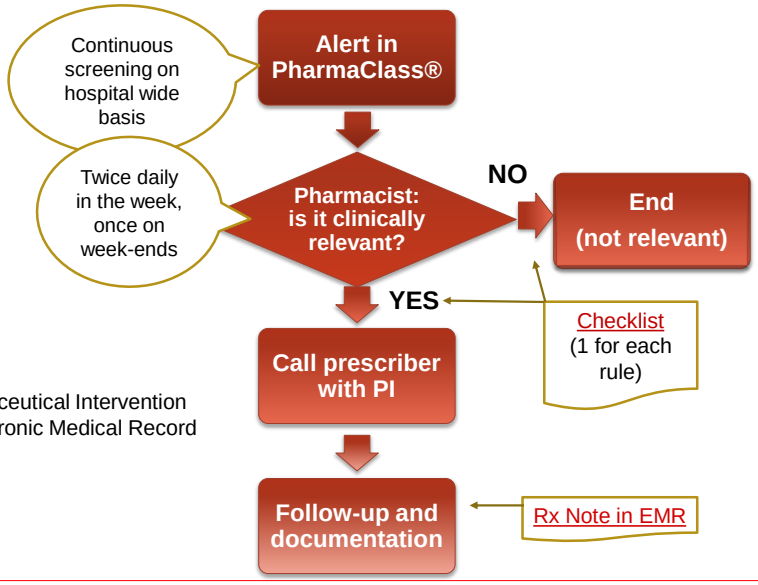
Check-list for Methotrexate :
- Indication (do not consider if used for chemotherapy)
- Control several lab values (ASAT, ALAT, Bilirubin, albumin, Hemoglobin, WBC, platelets, renal function)
- Perform interaction check
- Check for signs of toxicity (diarrhea, stomatitis, abdominal pain, infections, …)

Different types of alerts

Meropenem > 3 days
Pip/tazo > 3 day
… more to come…

Antibiotic Stewardship → transfer to Infectious Diseases team

How it works

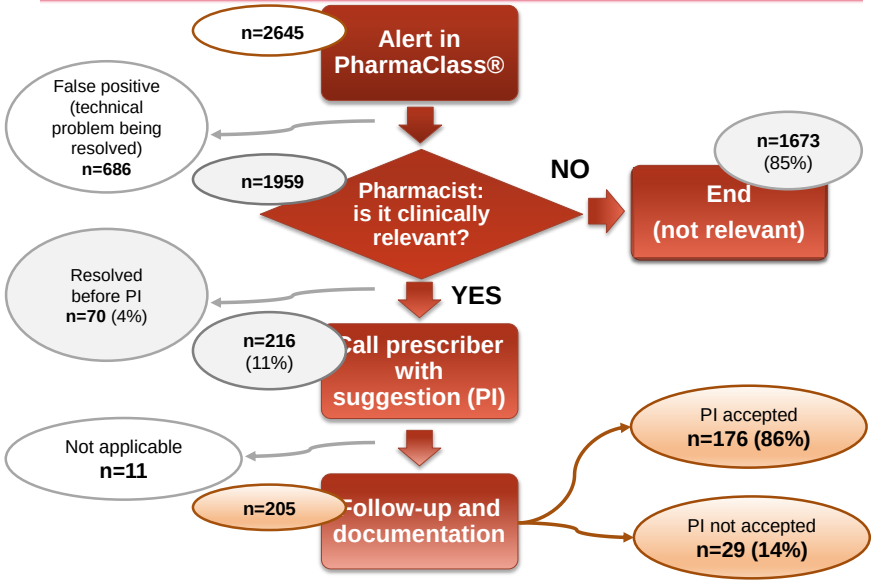


PI : Pharmaceutical Intervention
EMR : Electronic Medical Record

Why do the alerts go to the pharmacists ?

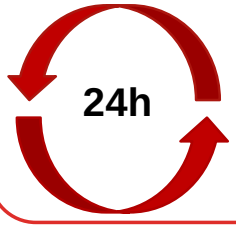
https://psnet.ahrq.gov/primers/primer/28/alert-fatigue (accès le 30.08.2019)

Results of 11 months



Indicators

Per Day:



Pharmacist time spent: 1h20

Risk situations analyzed: 10

1 Pharmacist Intervention of high criticality

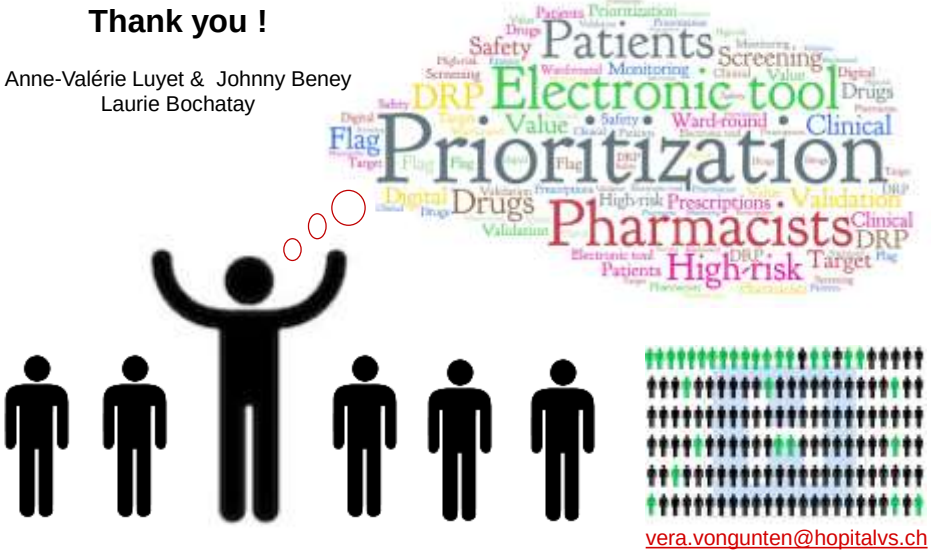
86% of PI will lead to a treatment modification

Is electronic screening Helpful or Harmful?

	HELPFUL	HARMFUL
INTERNAL	Strengths : - Coverage of more patients - Surveillance of high-risk drugs / clinical situations - Deployment of clinical pharmacy	Weaknesses : - Needs rules with high PPV - Limitations of IT tools - Depends on quality of documentation - Rx & IT time for system maintenance
EXTERNAL	Opportunities : - Drug use evaluations - ATB stewardship - Follow-up of high-cost drugs - National and international collaboration - Prepare ward rounds	Threats : - Failures/crashes of the information systems - Pharmacist accountability - Loss of interprofessionnal relationship ?

Thank you !

Anne-Valérie Luyet & Johnny Beney
Laurie Bochatay



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ANY QUESTIONS?

Patient prioritization : electronic tools

- **Roten** I, Marty S, Beney J. Electronic screening of medical records to detect inpatients at risk of drug-related problems. *Pharm World Sci*. 2010;32:103–107. http://dx.doi.org/10.1007/s11096-009-9352-6
- **Hickson** RP, Steinke DT, Skitterall C, Williams SD. Evaluation of a pharmaceutical assessment screening tool to measure patient acuity and prioritise pharmaceutical care in a UK hospital. *Eur J Hosp Pharm*. 2016;24:74–79.
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- **Cottrell** R, Caldwell M, Jardine G. Developing and implementing a pharmacy risk screening tool. *Hosp Pharm Eur*. 2013;71.
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- **Jeon** N, Staley B, Johns T, Lipori GP, Brumback B, Segal R, Winterstein AG. Identifying and characterizing preventable adverse drug events for prioritizing pharmacist intervention in hospitals. *Am J Health Syst Pharm*. 2017;74:1774–1783.
- **Mullan** N, Jennings A. Pharmacists' Use and Views of the Electronic Prescribing Web Portal. Paper presented at GHP/UKCPA 9th National Joint Conference, Harrogate, UK; 2013.
- **Munday** A, Forrest R. New Ways Of Pharmacy Team Working Within Acute Hospital Services in NHS Greater Glasgow & Clyde. *J Pharm Manag*. 2016;32:84–87.
- **Nguyen** T-L, Leguelinel-Blache G, Kinowski J-M, Roux-Marson C, Rougier M, Spence J, Le Manach Y, Landais P. Improving medication safety: Development and impact of a multivariate model-based strategy to target high-risk patients. *PLoS One*. 631 2017;12:e0171995.
- **Safadeh** M, Pazik L KR. A baseline assessment of the pharmaceutical needs of adult patients admitted to Stoke Mandeville Hospital. *Clin Pharm 2012*. 2012:S36–S38.

Alshakrah MA, *Research in Social & Administrative Pharmacy* (2018), doi: https://doi.org/10.1016/j.sapharm.2018.09.009.

Prescription de Méthotrexate

DESCRIPTION
Afin d'évaluer les effets indésirables et les interactions possibles

CONDUITE A TENIR:
- Vérifier l'indication
- Contrôler les transaminases hépatiques (ALAT, ASAT PAL, albumine, bilirubine), la numération sanguine (Hb, leucocytes, thrombocytes) et la fonction rénale (NB: autre alerte pour MTX et fonction rénale <60ml/min).
- Faire un check d'IA
- Et: réactions hématologiques (leucopénie, thrombopénie, anémie macrocytaire) et gastro-intestinales (stomatite, nausées, douleurs abdominales, diarrhées, hémorragies digestives), pneumonie, nodules rhumatoïdes/exanthème, infections, alopécie

Bibliographie:
Monitoring toutes les 2 à 4 semaines pendant 3 mois, puis toutes les 8 à 12 semaines pendant les 3 mois suivants, puis toutes les 12 semaines. Plus fréquemment en cas d'association avec un autre médicament hépatotoxique ou hématotoxique.

Interactions:
Aplasie médullaire: sulfamide antibactérien, triméthoprime, hydantoïne, dérivés des pyrazolés, chloramphénicol, sulfonylurées (déplacent le MTX de sa liaison avec l'albumine et augmente sa concentration plasmatique libre.
Interactions possibles avec les barbituriques, les tranquillisants, les tétracyclines, le furosémide, le probénécide et les anti-inflammatoires non-stéroïdiens.

www.swissmedicinfo.ch
https://www.rheuma-net.ch/fr/informations-a-propos/recommandations-patient
PIM Check N° 67

Prescription de vancomycine et taux résiduel de vancomycine hors norme

DESCRIPTION

Prescription de vancomycine et taux résiduel hors norme (< 10mg/L ou >20mg/L)

CONDUITE A TENIR

- Vérifier la pré-analytique
- Vérifier la fonction rénale (chez l'insuffisant rénal, la demi-vie est allongée). Considérer une amélioration ou une péjoration de la fonction rénale pour l'ajustement de dose
- En fonction du taux: proposer des adaptations de dose/intervalle ou rappeler au médecin de le faire
  - L'ajustement de la vancomycine n'est pas une science exacte, et les nomogrammes sont à titre indicatif
  - La vancomycine a une PK linéaire: doubler la dose pour doubler le taux; si la fonction rénale est stable

Bibliographie

Des taux < 10mg/L peuvent induire une résistance

Et mineurs: nausées, vomissements, douleurs musculaires, prurit, fièvre, éruption cutanée, hypokaliémie.

Et majeurs: ototoxicité, néphrotoxicité, arrêt cardiorespiratoire, hypotension, neutropénie, agranulocytose, thrombocytopénie.

https://www.gotarch.com/images/Vancomycin/DosageChart.pdf
www.swissethics.ch
https://pharmacie.hopitalvs.ch/pharmacieintranet/Annexes/Annexe-15_TDM_F_D_org_rw.pdf
https://www.universityhealthsystem.com/.../media/files/clinical-pathways/vancomycin-dosing-guidelines-adults-rev10-2014.pdf?la=en
Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health-Syst Pharm. 2009;66:82-98

Règles de criticité élevée: plusieurs catégories

1. Médicaments critiques à suivre

- Prescription de colchicine (afin d'évaluer les interactions et les effets indésirables)
- Prescription d'un immunosuppresseur
- Prescription de Mysoline° 250mg
- Prescription de méthotrexate (afin d'évaluer les interactions et les effets indésirables)

Règles de criticité élevée: plusieurs catégories

2. Problème médicamenteux probable

- Prescription de digoxine ET digoxinémie à taux toxique (>3nmol/L)
- Prescription de digoxine ET kaliémie hors norme (<3.5 ou >5.5mmol/L)
- Association d'azathioprine/ mercaptopurine et d'allopurinol/ febuxostat
- Prescription de méthotrexate et GFR<80ml/min
- Prescription de méthotrexate deux jours de suite
- Prescription de colchicine ET GFR< 30ml/min
- Prescription d'EPO plus d'une fois par semaine
- Prescription d'un inhibiteur direct du facteur Xa ET GFR< 15ml/min
- Prescription de dabigatran étexilate ET GFR<30ml/min
- Association de deux anticoagulants oraux
- Prescription de metformine ET GFR<30ml/min OU taux de lactate >5mmol/L
- Prescription de mycophénolate mofetil ET neutropénie (<1.3G/L)
- Prescription de morphine ET GFR<15ml/min (sauf soins palliatifs)
- Prescription de métamizole ET agranulocytose (neutrophiles < 0.5G/L)
- Association de carbamazépine et de clozapine
- Prescription de lévétiracétam et GFR<80ml/min
- Prescription de méthotrexate ET absence d'acide folique
- Prescription d'héparine (HNF ou HBPM) ET thrombocytopénie (=<50 G/L)
- Association de deux médicaments pouvant induire un syndrome sérotoninergique
- Prescription de vancomycine et taux résiduel hors norme (<10mg/L ou >20mg/L)

Règles de criticité élevée: plusieurs catégories

3. Antibiotic stewardship

- Prescription de méropénème durant >3jours