Workshop - Check of Medication Appropriateness (CMA): an instrument to implement guidelines in practice

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Disclosure

Relevant Financial Relationship None

Off-Label Investigational Uses
None

Interactive workshop

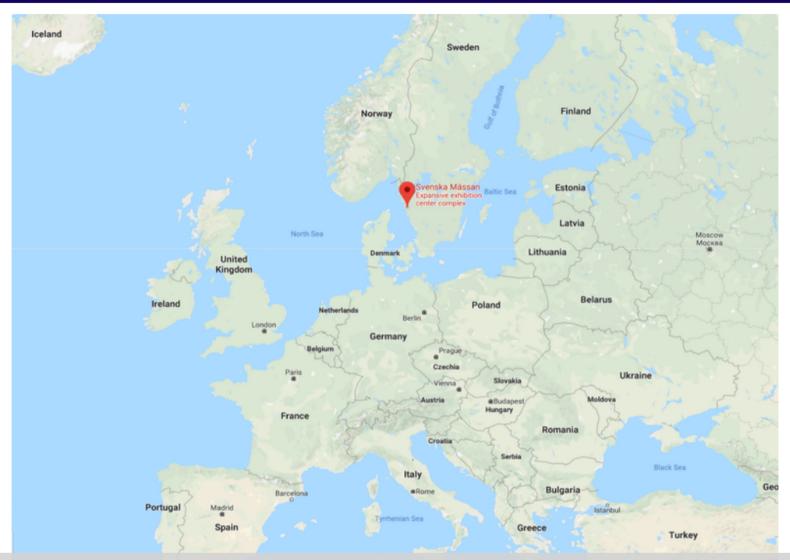
- Anonymous poll system
- Join us via



PollEv.com/thomasdr



Select the country where you work



Learning objectives

Understand how a CMA program works based on a case-based approach

- Understand how to set up a CMA program in your own hospital
- Understand how to prioritize the clinical rules covered by CMA





Content



Introduction

- Clinical pharmacy in general
- Clinical validation in general
- Clinical validation in University Hospitals Leuven



Clinical practice: how to start?

- Conditions
- Clinical input
- Impact



Advanced CMA on a case-based approach

- How to integrate evidence-based guidelines?
- How to build your own algorithms?



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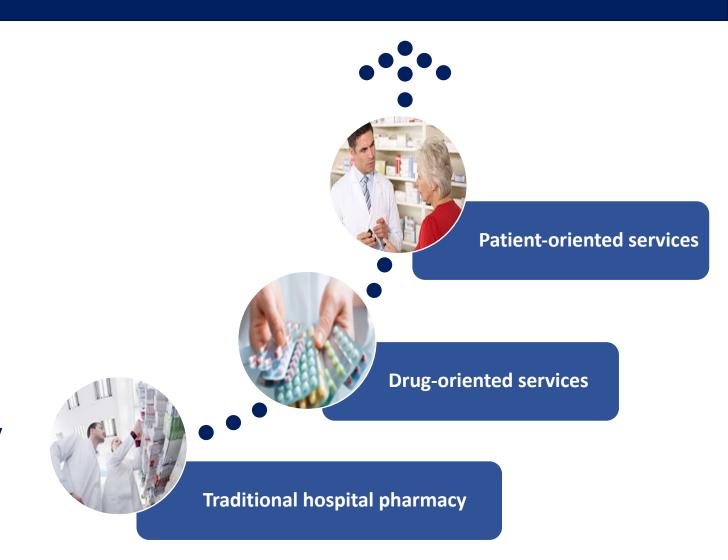
Advanced CMA on a case-based approach

- How to integrate evidence-based guidelines?
- How to build your own algorithms?

Introduction: clinical pharmacy in general

Shift in healthcare services

- USA/Canada/UK/Australia...:
 - Bedside clinical pharmacy implemented on all wards
- Limited resources in Belgian hospitals:
 - Only bedside clinical pharmacy on high risk wards







How many full-time working (FTE) pharmacists are employed in your hospital pharmacy?

< 1 FTE/ 100 BEDS 1 FTE / 100 BEDS

2 FTE / 100 BEDS > 2 FTE / 100 BEDS

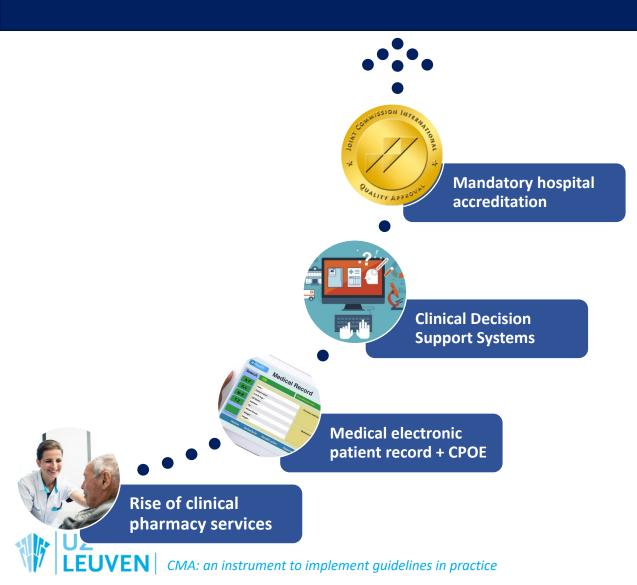
How many FTE's are available for clinical pharmacy?

< 1 FTE/ 200 BEDS 1 FTE / 200 BEDS

1 FTE / 300 BEDS

> 1 FTE / 300 BEDS

Introduction: clinical validation in general



Check of Medication Appropriateness

=

Clinical validation of prescriptions

→ BACK OFFICE CLINICAL PHARMACY



Quality + patient safety

How are clinical pharmacy services organized?

No clinical pharmacy

Only BACK-office clinical pharmacy

Only FRONT-office clinical pharmacy

BACK+FRONT office clinical pharmacy

What kind of clinical validation are you doing?

No validation

Basic

- Without access to the patient's medical record
- Posology

Intermediate

- Limited access to the patient's medical record
- Posology, indication, interactions, allergy...

Advanced

- Full access to the patient's medical record
- Indication, interactions, allergy...
- (Integrated)

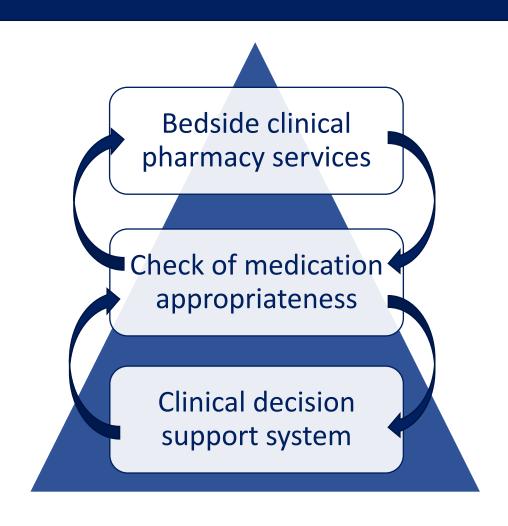
- Large hospital
 - 2000 beds, 5000 new prescriptions/day
 - 24,5 FTE
- Full medical electronic patient record
 - **CDSS**: drug-drug interactions, allergy, pregnancy, maximum dosage, therapeutic duplication
- **Bedside** clinical pharmacy on high risk wards:
 - Geriatrics
 - Abdominal surgery
 - Trauma surgery
 - Septic orthopedic
 - Pediatrics
- March 2016: implementation CMA





Target group:

- 1. For all patients potentially at risk for drug related problems
- 2. Evaluation at any time during hospitalization
- 3. Evaluation independently of drug dispensing





Method:

Based on maximum integration of structured data from patient file

Risk analysis to identify high risk prescriptions

Formulating
queries to screen
for high risk
prescriptions

Daily screening of all prescriptions generating a worklist

Validation by trained hospital pharmacists using standardized algorithms

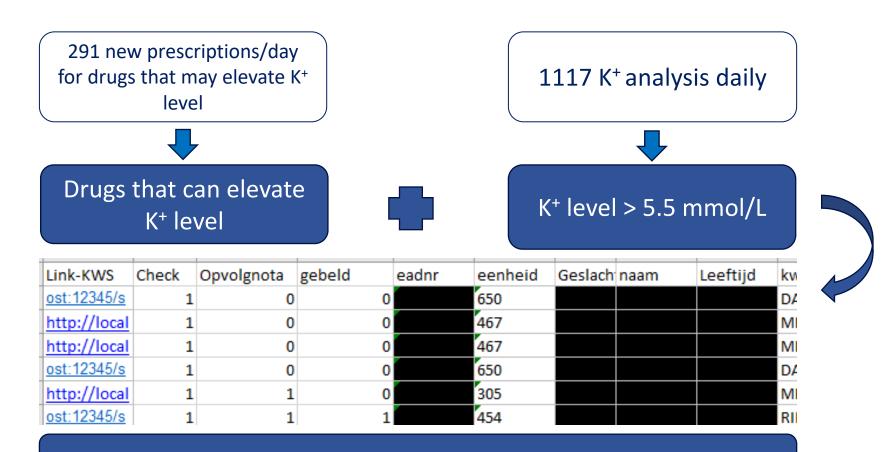
Interventions via electronic alerts or phone calls







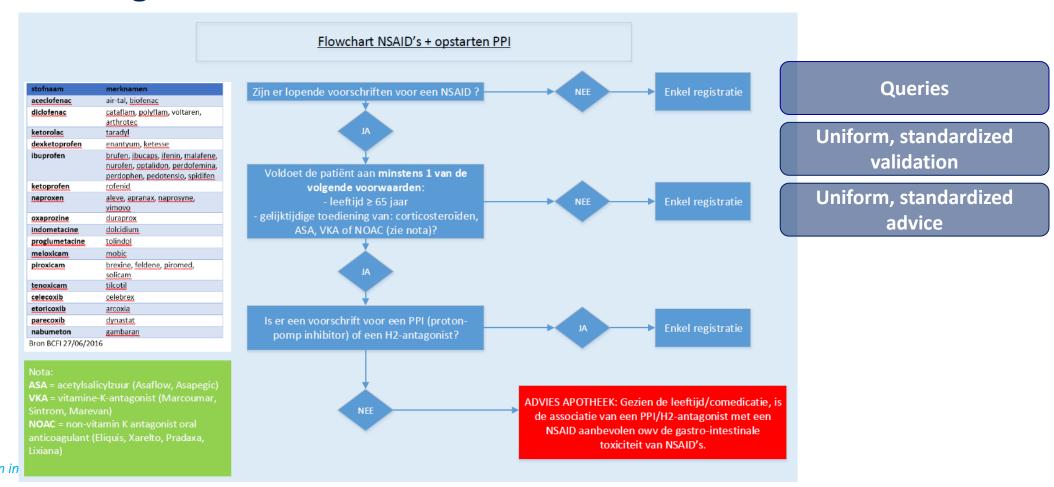
Maximum integration of structured data:



Worklist of 7 lines a day to be checked by a hospital pharmacist



Standardized algorithm:



• 79 specific algorithms covering 4 pharmacotherapeutic areas:

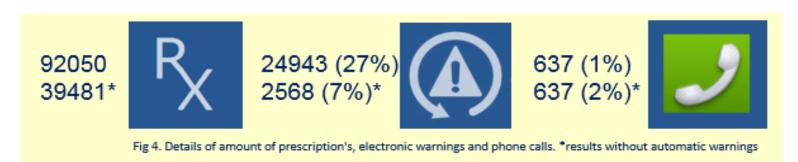
Drugs with restrictive indication or dosing

Medication-related biochemical changes

Evaluation of overruled interventions raised by CDSS

Sequential therapy for bio-equivalent drugs

• First results (March 2016-September 2017):



	Number of prescriptions checked (n)	Number of electronic notes (n (%))	Number of electronic notes + phone calls (n(%))
Drug use in renal insufficiency	9,381	444 (4.7%)	81 (0.9%)
Drugs with high potential of QT prolongation	4,223	608 (14.4%)	139 (3.3%)
Drugs with restrictive indication or dosing	5,276	448 (8.5%)	142 (2.7%)
Overruled severe DDIs	18,902	939 (5%)	259 (1.4%)





Example CMA:

Medication	8-1-2018	9-1-2018	10-1-2018
NaCl 0.9% (1,000 ml VIAFLO) IV	60 ml/uur	60 ml/uur	60 ml/uur
Pantoprazole (tabl 20 mg) oral	20 mg	20 mg	20 mg
Ondansetron (amp IV 4 mg/2 ml) IV	4x 4mg	4x 4mg	
Enoxaparine (20 mg/0.2 ml) SC	20 mg	20 mg	20 mg
Edoxaban (tabl 30 mg) oral	30 mg	30 mg	30 mg
Paracetamol (fl inj 500 mg/50 ml) IV	4x 500 mg	4x 500 mg	4x 500 mg
Haldol (amp inj 5 mg/1 ml) IV	2.5 mg	2.5 mg	2.5 mg
Quetiapine (caps 12.5 mg) oral	12.5 mg	12.5 mg	12.5 mg



Which checks would you do on this prescription?

Posology

Interactions

IV-PO switch

Contra-indications

Allergy

All checks

Medication 8-1-2018 NaCl 0,9% (fl inf 1,000ml VIAFLO) IV-inf 60 ml/uur Pantoprazole (tabl 20 mg) PO 20 mg Ondansetron Braun (amp IV 4mg/2ml) IV-bolus 4x 4mg Enoxaparine (20 mg/0.2ml) SC 20 mg Edoxaban (tabl 30 mg) 30 mg Paracetamol (fl inj 500mg/50ml) IV-inf 4x 500 mg Haldol (amp inj 5 mg/1ml) IV-inf 2.5 mg Quetiapine (caps 12.5mg) 12.5 mg

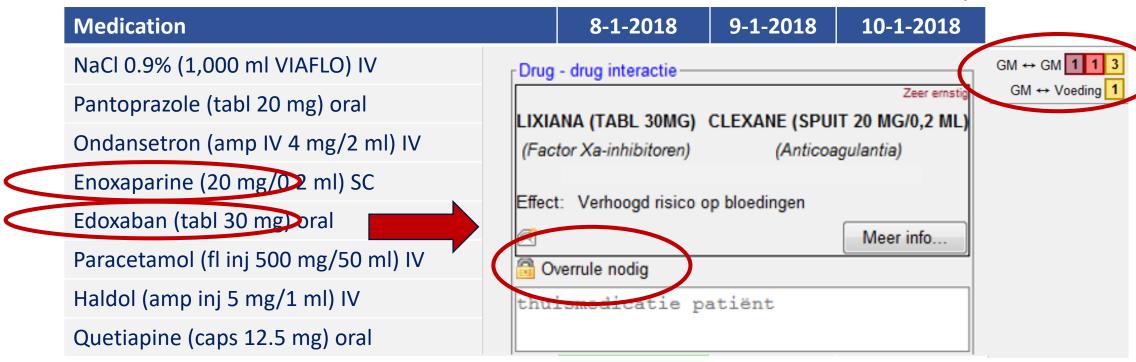
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1. Prescription of a very serious drug-drug interaction

Example CMA:

2. Alert generated by CDSS



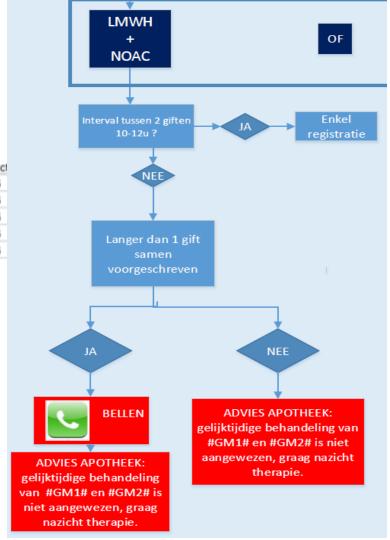
1. Prescription of a very serious interaction

Example CMA:

• In case of an **overrule** by the treating physician: **listed on the CMA worklist**

1	Link-KWS	Check	Opvolgnota	Opvolgnota-gebeld	eadnr	voorschrijver	sendTime	overruleInteract
32	http://localhost:1234						Jan 8 2018	DRUG_DRUG
33	http://localhost:1234						Jan 8 2018	DRUG_DRUG
34	http://localhost:1234						Jan 9 2018	DRUG_DRUG
35	http://localhost:1234						Jan 8 2018	DRUG_DRUG
36	http://localhost:1234						Jan 9 2018	DRUG_DRUG

 Validation of interaction by the pharmacist based on specific flowchart



Example CMA:

• Call to the treating physician + formulating an electronic alert in the patient's medical record





09-01-2018 16:40	TRH	ADVIES APOTHEEK: gelijktijdige behandeling van Lixiana en Clexane is niet aangewezen, graag nazicht therapie.
09-01-2018 16:40	TRH	 ADVIES APOTHEEK: De dosis van Lixiana wordt aangepast aan patiëntenkarakteristieken (nierfunctie, en/of gewicht). Graag nazicht therapie.

• Result:

Medication	8-1-2018	9-1-2018	10-1-2018
NaCl 0.9% (1,000 ml VIAFLO) IV	60 ml/uur	60 ml/uur	60 ml/uur
Pantoprazole (tabl 20 mg) oral	20 mg	20 mg	20 mg
Ondansetron (amp IV 4 mg/2 ml) IV	4x 4mg	4x 4mg	
Enoxaparine (20 mg/0.2 ml) SC	20 mg	20 mg	20 mg
Edoxaban (tabl 30 mg) oral	30 mg	30 mg	30 mg





Clinical practice: how to start?

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POLICY

TOOLS



POLICY

• In relation with **drug dispensing**:

Drug dispensing depending on clinical validation



Validation of drugs before delivery



- Deadline stress
- Low performance
- Missing decentralized drug dispensing

Independent services

- High performance
- Check decentralized drug dispensing

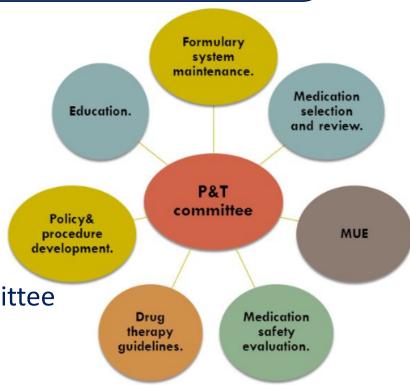
Administration of drugs before validation



CMA: an instrument to implement guidelines in practice

POLICY

- Multidisciplinary collaboration:
 - Hospital Board
 - Hospital wide communication newsletter
 - Reporting results
 - Pharmaceutical and Therapeutics (P&T) Committee
 - Identifying high risk prescriptions
 - Validation (of algorithms)
 - Medical Ethics committee
 - Law on Patients' Rights
 - Other committees: e.g. Antimicrobial stewardship committee
 - → Hospital-wide support
 - Relevant national professional associations
 - Partner Hospitals

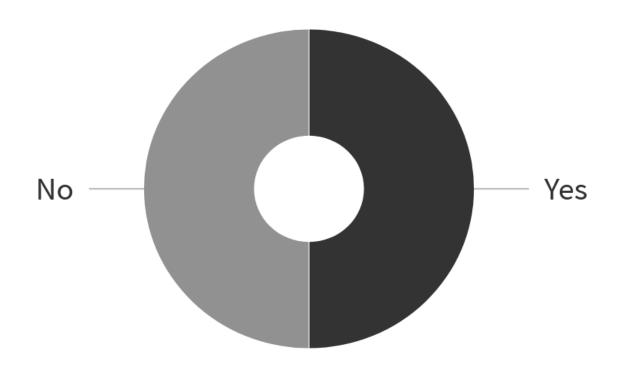






Do hospital pharmacists actively participate in committees?





POLICY

Accreditation:

- JCI
- NIAZ Qmentum



Human resources:

- How many FTE employing on clinical validation?
- All hospital pharmacists, or only clinical educated hospital pharmacists?





How many FTE's are employed for clinical validation?

O FTE

0,5 FTE

0,5-1 FTE

> 1 FTE

- **Necessities** to do intermediate/advanced clinical validation:
 - Medical electronic patient record
 - CPOE
- Added values
 - Clinical Decision Support Systems (CDSS)
 - (Drug-drug) interactions
 - Maximum doses
 - Drug use during pregnancy/lactation
 - Therapeutic duplication
 - Allergy
 - ...
 - Artificial Intelligence





How to start: conditions

TOOLS

- Registration of interventions + registration of acceptability
 - Traceability
 - Documenting clinical service
 - Hospital Board
 - Accreditation
 - Evaluating & optimizing the service



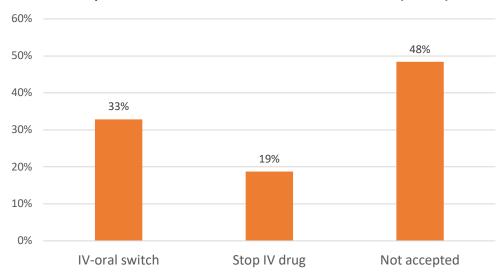


How to start: conditions

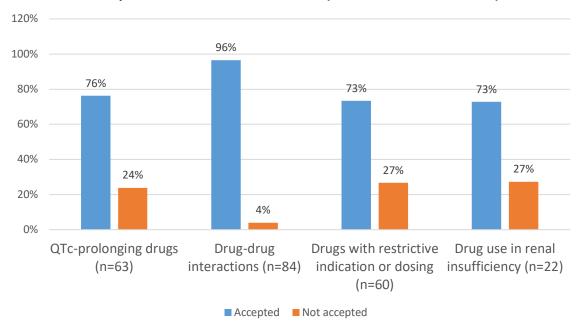
TOOLS

- Acceptance rate
 - Preliminary results

Acceptance rate of interventions for IV-oral switch (n=320)



Acceptance rate CMA interventions (other than IV-oral switch)

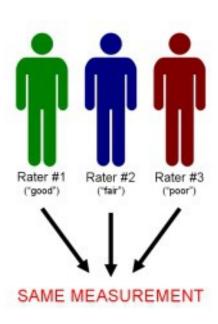


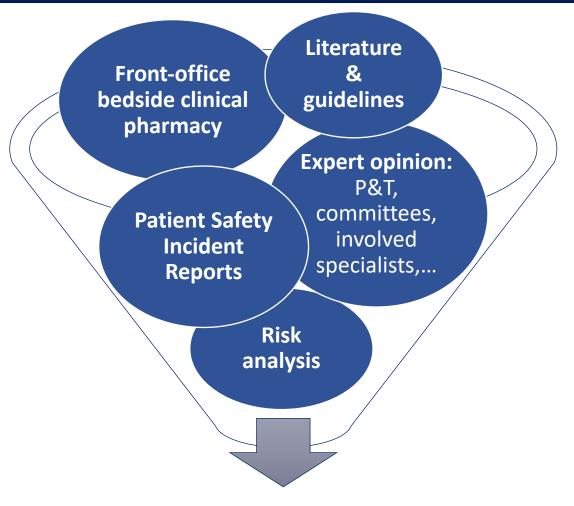


How to start: conditions

TOOLS

- Education of hospital pharmacists
 - Start-up training for all pharmacists
 - Continuous learning and retraining of new guidelines
 - E-learning modules
 - Clinical pharmacy => inter pharmacist variability
 - How much homogeneity in the validation done by different pharmacists?
 - → Interrater reliability







Case:

- Female, 84 y, 52 kg
- Geriatrics
- Diagnosis: Urinary tract infection & delirium
- Medical history: Afib, Diabetes Mellitus type 2, Chronic Renal Insufficiency (CrCl 22 ml/min)
- Microbiology:
 - E.coli: sensitive to fluoroquinolones and beta-lactam antibiotics
 - Clostridium difficile +

Prescribed medication

Amoxicillin/clavulanic acid oral 850/125 mg dt q8h

Apixaban oral 5 mg dt q12h

Zolpidem oral 10 mg dt q24h

Metformin oral 850 mg dt q8h

Paracetamol IV 1g dt q6h

Carbamazapine oral 200 mg dt q12h

Which checks would you do on this prescription?

Posology

Renal function

Drug-drug interactions

IV-oral switch

Intreated indications

Microbiology

Other

All

Prescribed medication

Amoxicillin/clavulanic acid oral 850/125 mg dt q8h

Apixaban oral 5 mg dt q12h

Zolpidem oral 10 mg dt q24h

Metforming oral 850 mg dt q8h

Paracetamol IV 1g dt q6h

Carbamazapine oral 200 mg dt q 12h

A. POSOLOGY (standard)

- Amoxicillin/clavulanic acid
 - UTI: e.g. ESCMID guidelines⁽¹⁾



- Afib: e.g. ESC guidelines^(2,3)
- Standard dosing Afib: 2x 5 mg
- Posology based on indication, weight, renal function and age

Carbamazepine

Standard dosing: 100 -1200 mg/day

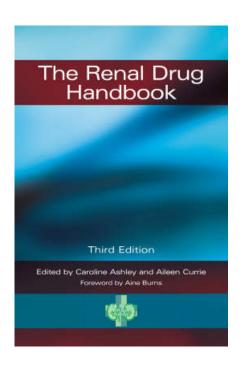






B. RENAL FUNCTION

- Dose adjustments to renal function:
 - Amoxicillin/clavulanic acid
 - Apixaban⁽¹⁾
 - Metformin⁽²⁾
- Guidelines:
 - Renal Drug Handbook⁽²⁾
 - Clinicalpharmacology.com
 - Summary of product characteristics (SmPC)



C. Interactions

- Apixaban + carbamazepine⁽¹⁾
 - CYP3A4 substrate + CYP inducer
 - Decrease in serum concentration of apixaban
 - Effect on apixaban plasma level (AUC): 54%
 - Contraindication for simultaneous use

• Interactions:

• Interaction database: e.g. UpToDate.com (Lexicomp®), Clinicalpharmacology.com





D. IV-ORAL switch

- Paracetamol IV?
 - Bio-equivalent drug?
 - Intact gastrointestinal tract?
 - Ability to swallow?
 - Prescription for other oral medication
 - Food consumption
 - Without planned surgical procedures

E. Untreated indications

- Clostridium difficile infection (CDI)
 - IDSA guidelines⁽¹⁾, ESCMID guidelines⁽²⁾
 - Diagnosis: presence of symptoms + stool test positive for toxins
 - Treatment

Table 1. Recommendations for the Treatment of Clostridium difficile Infection in Adults

Clinical Definition	Supportive Clinical Data	Recommended Treatment ^a	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of ≤15000 cells/mL and a serum creati- nine level <1.5 mg/dL	 VAN 125 mg given 4 times daily for 10 days, OR FDX 200 mg given twice daily for 10 days Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days 	Strong/High Strong/High Weak/High
Initial episode, severe ^b	Leukocytosis with a white blood cell count of ≥15000 cells/mL or a serum creati- nine level >1.5 mg/dL	 VAN, 125 mg 4 times per day by mouth for 10 days, OR FDX 200 mg given twice daily for 10 days 	Strong/High Strong/High





PCR Clostridium
difficile positive
and toxine
positive

'Diarrhea' recorded in patient file

Presence of symptoms + stool test positive for toxins



NO treatment for Clostridium / difficile in CPOE NO prescripton for oral vancomycin or IV/oral metronidazole or oral fidaxomicin

Link-KWS	Check	Opvolgnota	gebeld	eadnr	eenheid	Geslach	naam	Leeftijd	kw
ost:12345/s	1	Opvoignota 0	0	Cadill	650	Gestacii	IIddiii	Leertija	DA
http://local	1	0	0		467				MI
http://local	1	0	0		467				MI
ost:12345/s	1	0	0		650				DA
http://local	1	1	0		305				MI
ost:12345/s	1	1	1		454				RII

On worklist to be checked by a hospital pharmacist



- F. Allergy
- Penicillin allergy?



G. Microbiology

- UTI
 - Betalactam antibiotics inferior to fluoroquinolones? ESCMID guidelines(1)
- Local guidelines > Antibiotic policy committee





Which check is the most important?

IV-oral switch paracetamol

Posology - antibiotic, NOAC and carbamazepine

Untreated indications (CDI)

Allergy - penicillins

Microbiology

Renal function antibiotic, NOAC, metformin

Prescribed medication

Amoxicillin/clavulanic acid oral 850/125 mg dt q8h

Apixaban oral 5 mg dt q12h

Zolpidem oral 10 mg dt q24h

Metforming oral 850 mg dt q8h

Paracetamol IV 1g dt q6h

Carbamazapine oral 200 mg dt q 12h

How to start: measuring impact

- Acceptance rate
- Clinical relevance
- Satisfaction survey
- Economic analysis

→ Important to keep:

evaluating the service defining new goals & developing new checks optimizing the service & improving performance







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Advanced CMA on a case-based approach

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Case:

- Female, 81 y, 75 kg
- Admitted on trauma surgery because of a hip fracture

MEDICAL HISTORY
Arterial hypertension
Depression
Gastroesophageal reflux disease (GERD)
Hypothyroidism
Episode of atrial fibiliation (Afib)

LAB RES	ULTS
Parameter	Result
eGFR	57 mL/min
Potassium	3.71 mmol/L
Blood pressure	13/9 mmHg
Heart rate	81 BPM
TSH (0.27-4.2 mIU/L)	0.75 mIU/L
T4 (12-22 pmol/L)	0.75 pmol/L

Medication (CPOE)
Pantoprazole oral 20 mg, q24h
Amlodipine oral 5 mg, q24h
Bisoprolol oral 2.5 mg, q24h
Calcium-vitamin D oral 1000 mg-800 IE, q24h
Levothyroxine oral 50 mcg, q24h
Escitalopram oral 10 mg, q24h
Lormetazepam oral 1 mg, q24h





Are there drug-drug interactions?

Yes

Medication (CPOE)

Pantoprazole oral 20 mg, q24h

Amlodipine oral 5 mg, q24h

Bisoprololoral 2.5 mg, q24h

Calcium-vitamin D oral 1000 mg-800 IE, q24h

Levothyroxine oral 50 mcg, q24h

Escitalopram oral 10 mg, q24h

Lormetazepamoral 1 mg, q24h

No



Are there drugs that need a dose adjustment based on the lab results

yes

Medication (CPOE)
Pantoprazole PO 20 mg, q24h
Amlodipine PO 5 mg, q24h
Bisoprolol PO 2.5 mg, q24h
Calcium-vitamin D PO 1000 mg-800 IE, q24h
Levothyroxine PO 50 mcg, q24h
Escitalopram PO 10 mg, q24h
Lormetazepam PO 1 mg, q24h

Parameter	Result
eGFR	57 mL/min
Potassium	3.71 mmol/L
Blood pressure	13/9 mmHg
Heart rate	81 BPM
TSH (0.27-4.2 mIU/L)	0.75 mIU/L
T4 (12-22 pmol/L)	0.75 pmol/L

no



Does the patient have a contra-indication for some of the drugs?

Yes

MEDICAL HISTORY	Medication (CPOE)
Arterial hypertension	Pantoprazole PO 20 mg, q24h
Depression	Amlodipine PO 5 mg, q24h
Gastroesophageal reflux	Bisoprolol PO 2.5 mg, q24h
disease (GERD)	Calcium-vitamin D PO 1000 mg-800 IE, q24h
Hypothyroidism	Levothyroxine PO 50 mcg, q24h
Episode of atrial fibiliation	Escitalopram PO 10 mg, q24h
(Afib)	Lormetazepam PO 1 mg, q24h

No



In conclusion, can the therapy be validated as safe?

Yes

Medication (CPOE)

Pantoprazole PO 20 mg, q24h

Amlodipine PO 5 mg, q24h

Bisoprolol PO 2.5 mg, q24h

Calcium-vitamin D PO 1000 mg-800 IE, q24h

Levothyroxine PO 50 mcg, q24h

Escitalopram PO 10 mg, q24h

Lormetazepam PO 1 mg, q24h

No

In conclusion, can the therapy be validated as safe?





Which is the untreated indication?

Untreated indication:







Anticoagulant therapy to prevent stroke



How to **build your own algorithm** to screen for untreated Afib?



How to integrate evidencebased guidelines?



How to **build your own algorithm** to screen for untreated Afib?

1st step:

• Screen for patients, currently hospitalized, with <u>a proven diagnosis of Afib</u> (reported in ECG protocols)

How to **build your own algorithm** to screen for untreated Afib?

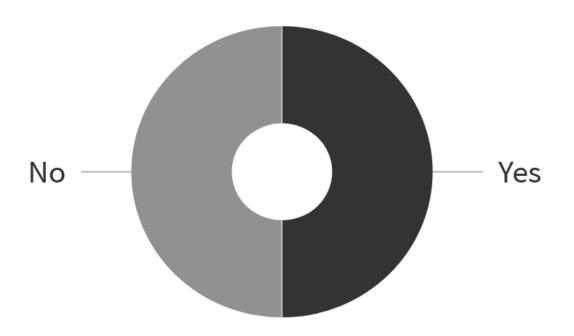
2nd step:

- Screen for patients, currently hospitalized, with a proven diagnosis of Afib
- AND who do need anticoagulant therapy



Does every patient, currently hospitalized, with a proven diagnosis of Afib need to be treated with anticoagulant therapy?





How to **build your own algorithm** to screen for untreated Afib?

Does every patient, currently hospitalized, with a proven diagnosis of Afib need to be treated with anticoagulant therapy?

No



Based on the risk for stroke (CHA₂DS₂-VASc score)

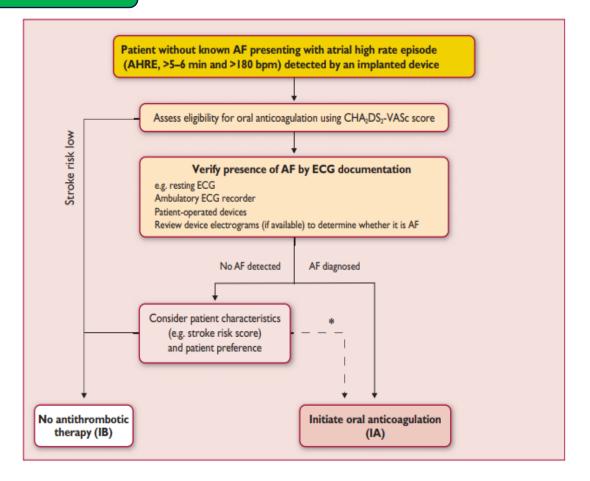
ESC guideline: Atrial Fibrillation Management



ESC guideline: Atrial Fibrillation Management

9. Stroke prevention therapy in atrial fibrillation patients

OAC therapy can prevent the majority of ischaemic strokes in AF patients and can prolong life. 38,39,42,194,201,329,350–352 It is superior to no treatment or aspirin in patients with different profiles for stroke risk. 353,354 The net clinical benefit is almost universal, with the exception of patients at very low stroke risk, and OAC should therefore be used in most patients with AF (Figure 8). Des-



ESC guideline: Atrial Fibrillation Management

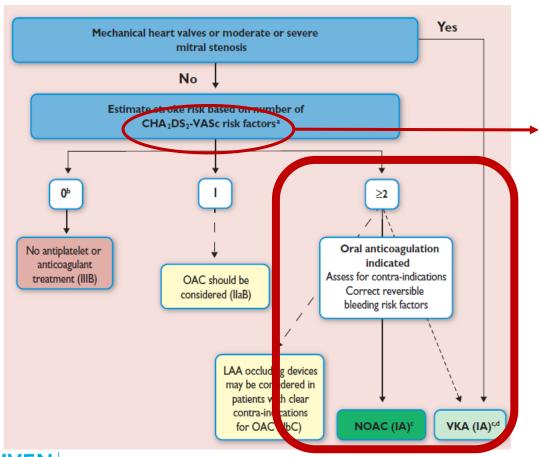


Table 11 Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism in the CHA₂DS₂-VASc score

CHA ₂ DS ₂ -VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left ventricular ejection fraction	+1
Hypertension Resting blood pressure > 140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	+1
Age 65-74 years	+1
Sex category (female)	+1

 CHA_2DS_2 -VASc = Congestive Heart failure, hypertension, Age \geq 75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female).



How to **build your own algorithm** to screen for untreated Afib?

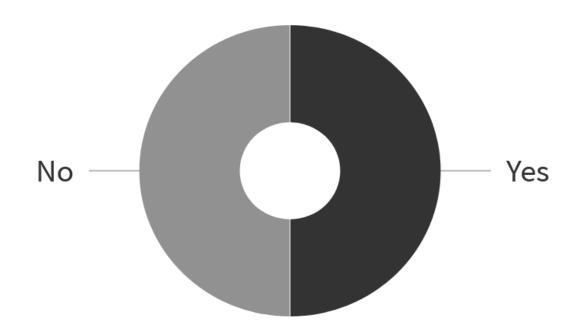
2nd step:

- Screen for patients, currently hospitalized, with a proven diagnosis of Afib
- AND who do need anticoagulant therapy based on the CHA₂DS₂-VASc score
 - In practice: calculation based on registered care paths and/or ATC codes
 - In case: > 75 y (2) + arterial hypertension (1) + woman (1) = 4



Does the algorithm need to select currently hospitalized patients who ever had a proven diagnosis of Afib and a CHA2DS2-VASc score of \geq 2?

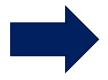




How to **build your own algorithm** to screen for untreated Afib?

Does the algorithm need to select, currently hospitalized patients who ever had a proven diagnosis of Afib and a CHA₂DS₂-VASc score of ≥ 2 ?

No



Only patients without a prescription for anticoagulant therapy

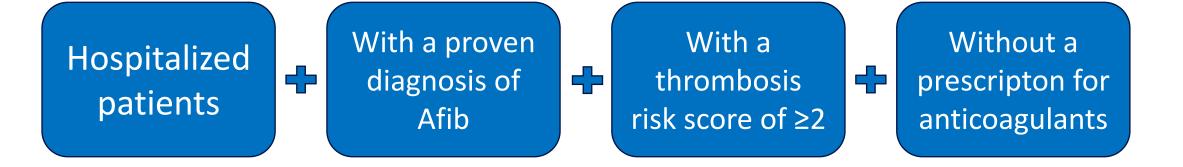
How to **build your own algorithm** to screen for untreated Afib?

3rd step:

- Screen for patients, currently hospitalized, with a proven diagnosis of Afib
- AND who do need anticoagulant therapy based on the CHA₂DS₂-VASc score
- AND without a prescription for anticoagulants

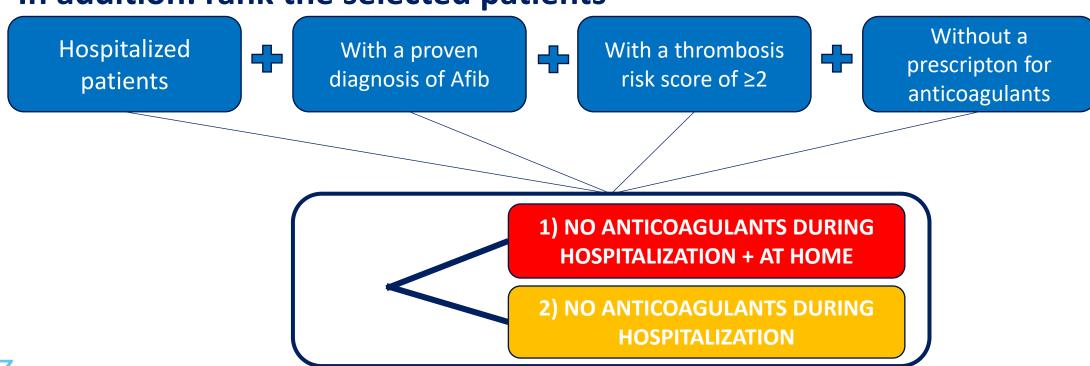
How to **build your own algorithm** to screen for untreated Afib?

CONCLUSION: Algorithm needs to screen for



How to **build your own algorithm** to screen for untreated Afib?

In addition: rank the selected patients





Take home messages

- 1. Clinical validation can operate as a **liaison between CDSS and bedside clinical pharmacy**
- 2. Screen for prescriptions with a high risk of drug related problems
- 3. Clinical input for the validation service needs to be based on
 - (Inter)national guidelines
 - Gained bedside knowledge
 - Local patient safety incident reports
 - Expert opinions
- 4. Hospital-wide support is essential (hospital board, IT, P&T, experts...)



Thank you for your attention

Call for feedback

