Evaluation of a Drug Safety Algorithm for the Detection of Triple Whammy prescriptions in inpatients at risks of acute Kidney Injury

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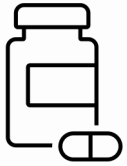
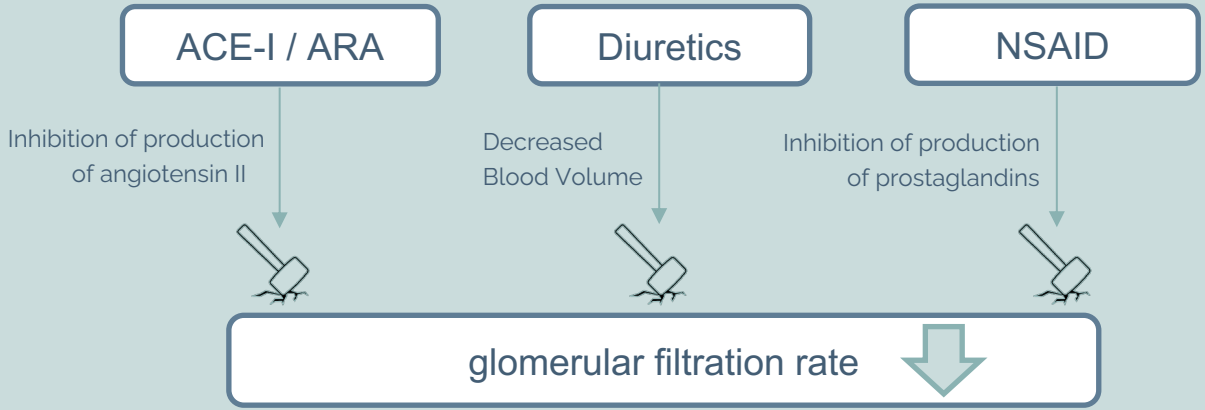
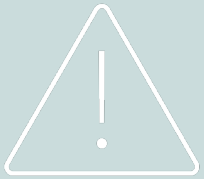
TRIPLE WHAMMY



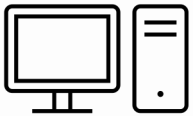




- Increases risk of Acute Kidney Injury (AKI) by 31%[1]

[1]Lapi F et al. *BMJ*. Jan 08 2013;346:e8525. doi:10.1136/bmj.e8525

MULTI-AGENTEN SYSTEM

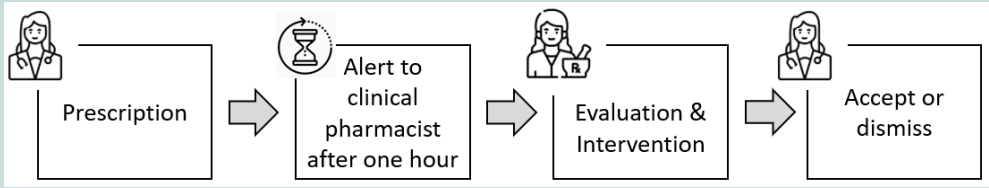


TRIPLE WHAMMY ALGORITHM

- **Alert 1**: Triple Whammy and eGFR < 30 ml/min/1.73m²
- **Alert 2**: Triple Whammy and eGFR between 30-60 ml/min/1.73m²
- **Alert 3**: Triple Whammy and age ≥ 75 years
- **Alert 4**: Triple Whammy without recent creatinine-measurements

INTERVENTIONS

- Stop NSAIDs or low dose/short duration
- Frequent measurements of creatinine (2x weekly)



Aim: Evaluation of algorithm

Clinical Pharmacists

Acceptable alert burden?
Sensitivity and Specificity?

Alerts 2021

Physicians

Acceptance Rate?
Satisfaction with algorithm?

Semi-structured Interviews

Patients

Detection of patients at risk?
Influence on kidney function?

Patients with Triple Whammy 2021

Clinical Pharmacists

- 333 alerts in 2021 for 210 patients*
- 254 alerts were processed by clinical pharmacists
- 110 (43.3%) messages were sent to physicians

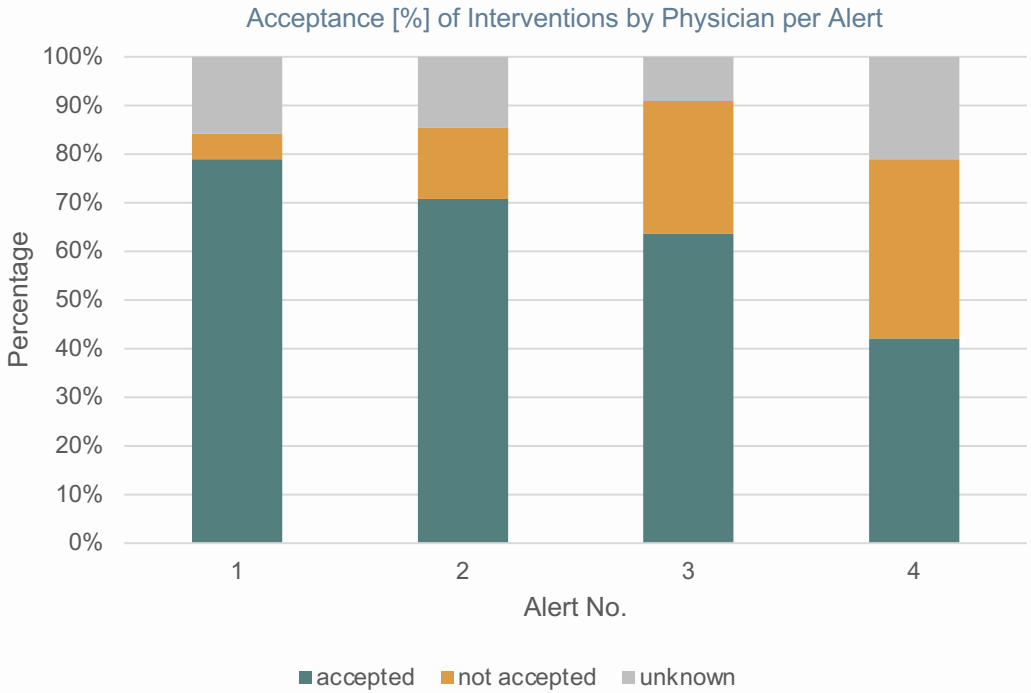
	Detection necessary	Detection unnecessary	total
Alert	144	66	210
No alert	19	21’097	21’116
total	163	21’163	21’326

Sensitivity
88.3%

Specificity
99.7%

*Excluding patients who received error messages

Physicians



Triple Whammy and..

Alert 1: eGFR < 30 ml/min/1.73m^2
Alert 2: eGFR between 30-60 ml/min/1.73m^2
Alert 3: age ≥ 75 years
Alert 4: No recent creatinine-measurements

- Overall acceptance rate 77.7% (73 von 94)
- Acceptance rate varies and increases with priority

INTERVIEWS WITH PHYSICIANS

25% 3 out of 12

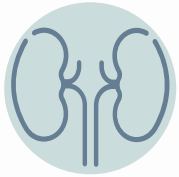
Know about the risk of Triple Whammy prescription

100% 11 out of 11

Consider the algorithm helpful and useful

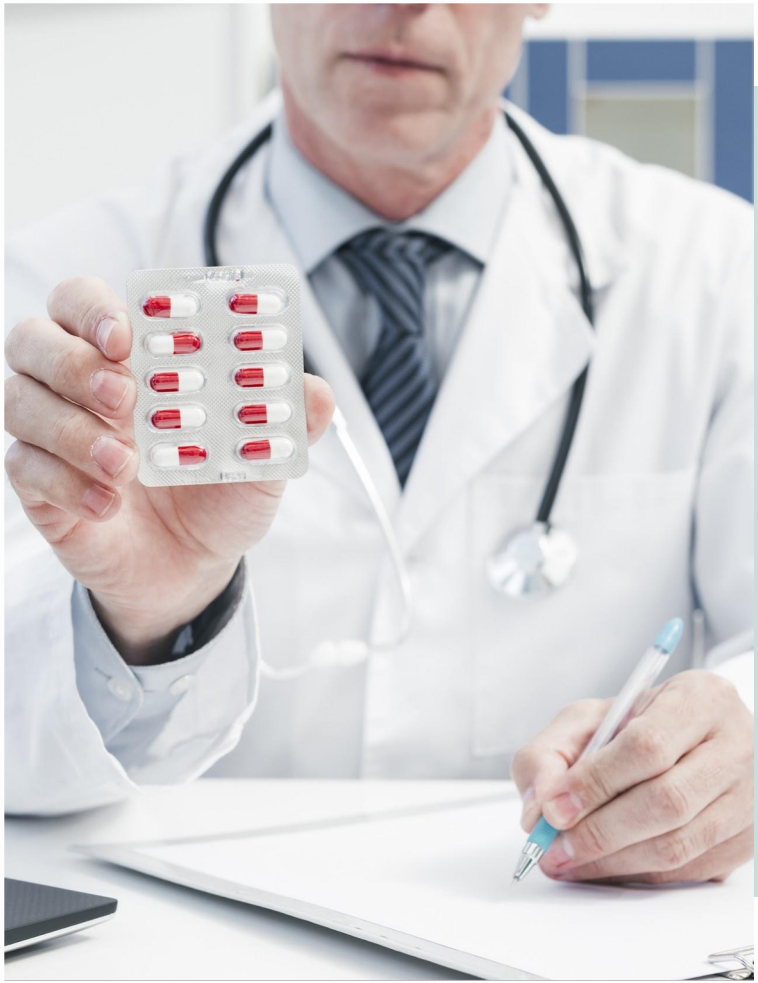
80% 8 out of 10

Will avoid a Triple Whammy prescription in the future



PATIENTS

- In 2021 we identified 290 Triple Whammy prescriptions in 21'326 patients (1.4%)
- 19 patients had an accepted intervention and never received a Triple Whammy
- 17 patients had an AKI* under Triple Whammy prescription
  - 15 patients received an alert
  - 2 Patients did not (Age 60 and 65 and normal eGFR at baseline)



Amount of Triple Whammy Alerts is reasonable, pharmacists can manage the number well.

High specificity and sensitivity achieved, no "alert fatigue" detected

High acceptance rates, physicians are satisfied with the algorithm

15/17 Patients with AKI under Triple Whammy detected

MERCI!

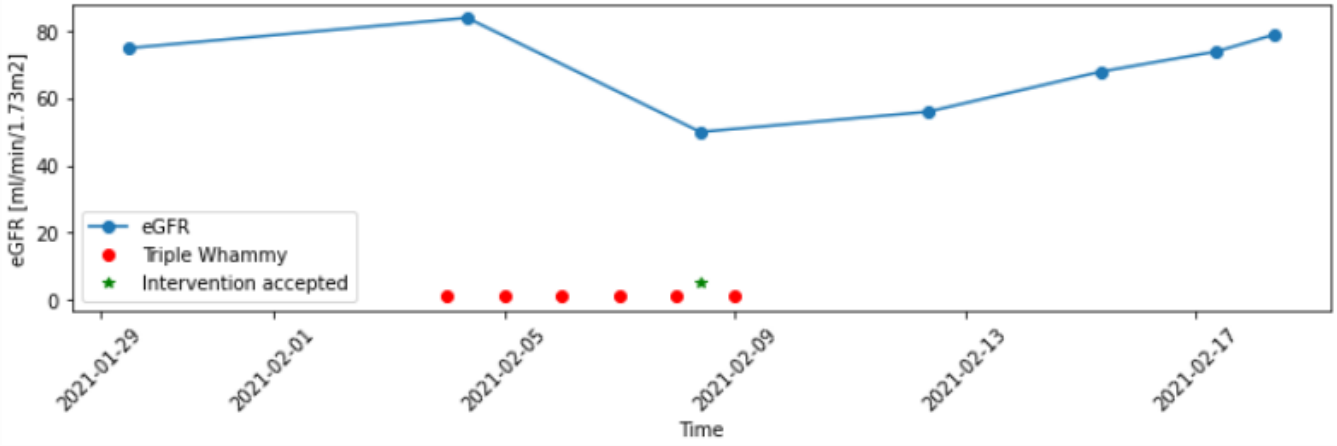
Masterarbeit: Jana Schelshorn

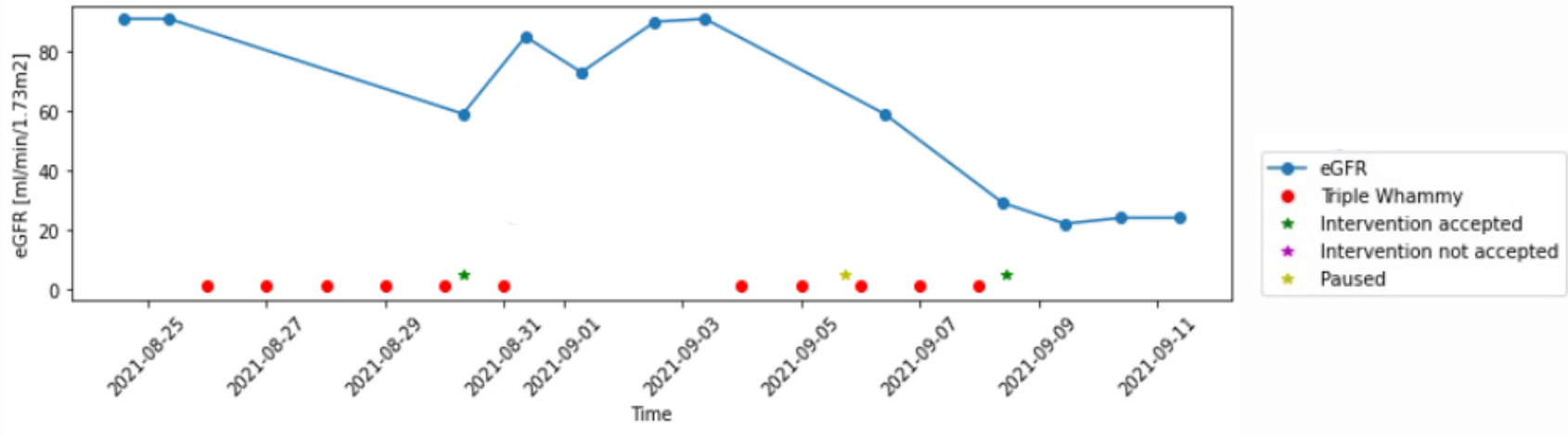
Betreuung: Claudia Zaugg, Carla Meyer-Massetti

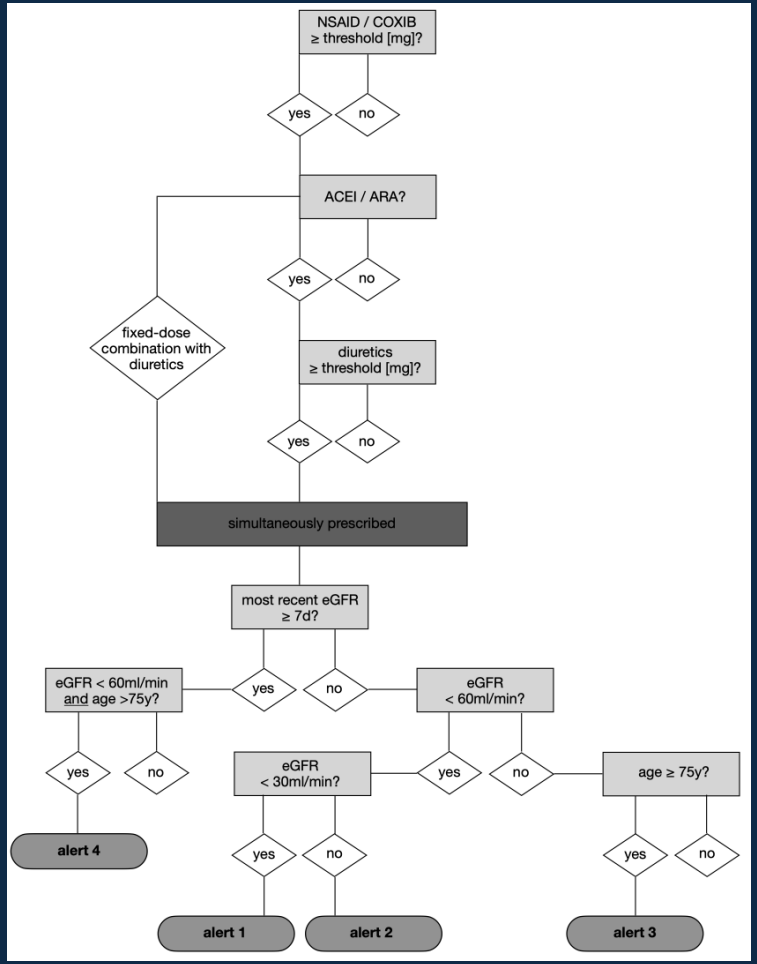
Entwicklung Algorithmus: Francisco Cabrera, Ali Reza Salili, Claudia Zaugg, Ricco Fiumefreddo, Philipp Schuetz

Outlook

- Implementation of dynamic kidney injury
- Adjust age as a trigger
- Discuss pausing-behavior amongst pharmacists
- Educate physicians about Triple Whammy
- Demonstrate an impact on patient safety with another study design


eGFR [ml/min/1.73m2]
0
20
40
60
80
eGFR
Triple Whammy
Intervention accepted
2021-01-29
2021-02-01
2021-02-05
2021-02-09
2021-02-13
2021-02-17
Time


eGFR [ml/min/1.73m2]
0
20
40
60
80
2021-08-25
2021-08-27
2021-08-29
2021-08-31
2021-09-01
2021-09-03
2021-09-05
2021-09-07
2021-09-09
2021-09-11
Time
eGFR
Triple Whammy
Intervention accepted
Intervention not accepted
Paused

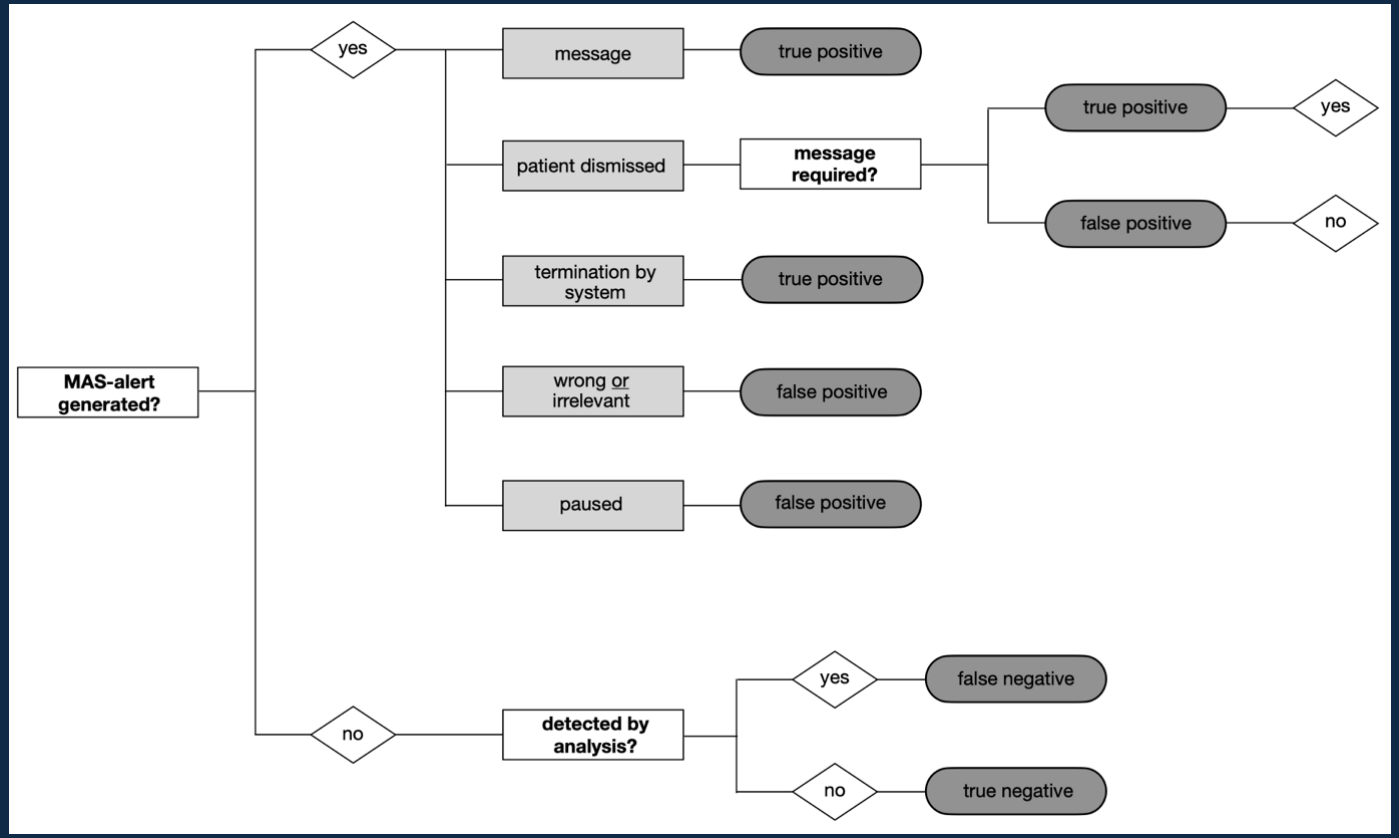

NSAID / COXIB
≥ threshold [mg]?
yes
no
ACEI / ARA?
yes
no
fixed-dose combination with diuretics
diuretics
≥ threshold [mg]?
yes
no
simultaneously prescribed
most recent eGFR
≥ 7d?
eGFR < 60ml/min
and age >75y?
yes
no
eGFR
< 60ml/min?
yes
no
yes
no
eGFR
< 30ml/min?
yes
no
age ≥ 75y?
yes
no
alert 4
yes
no
alert 1
alert 2
yes
no
alert 3

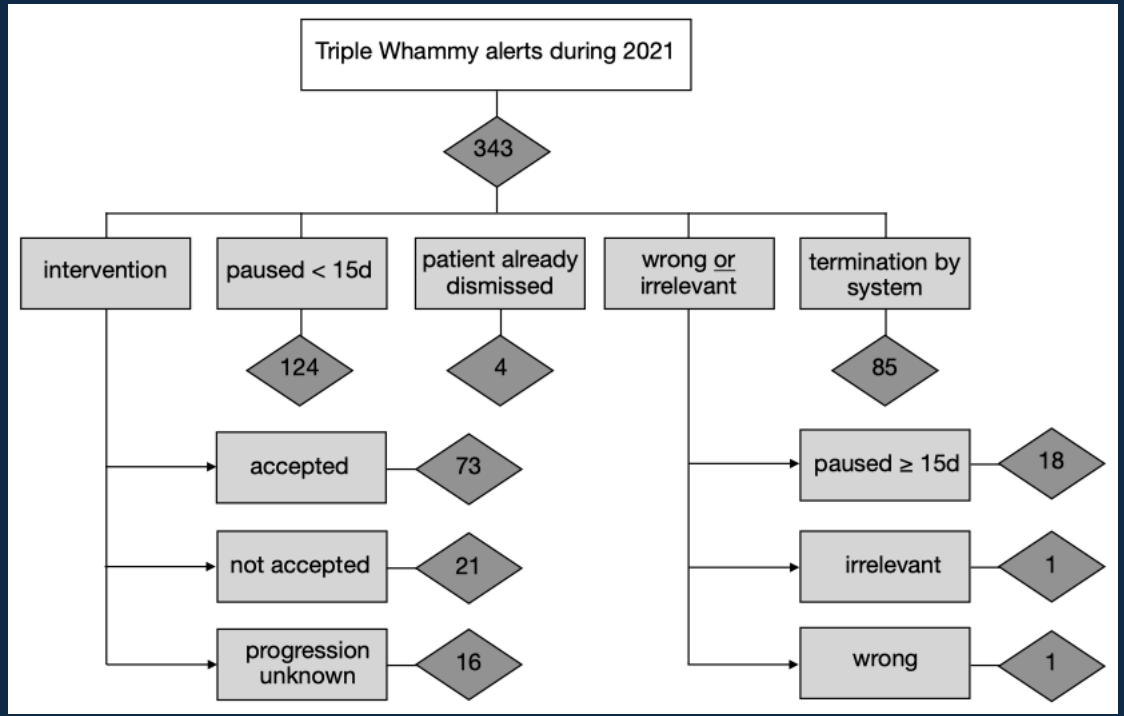
Age	
median [years]	77
.25 quartile [years]	67
.75 quartile [years]	83
18-34 years [number of patients]	**0.5%** (1)
35-54 years [number of patients]	**8.3%** (18)
55-74 years [number of patients]	**31.5%** (68)
75-84 years [number of patients]	**40.3%** (87)
>85 years [number of patients]	**19.4%** (42)
Sex [number of patients]	
female	**51.9%** (112)
male	**48.1%** (104)
Medication	
prescribed drugs [number of drugs]	21 ± 8
nephrotoxic medication [number of patients]	**14.8%** (32)
creatinine falsifiers [number of patients]	**3.2%** (7)
Duration Of Hospitalisation	
mean ± standard deviation [d]	7.1 ± 6.5
Hospital Ward [number of patients]	
surgery	**35.6%** (77)
orthopaedics	**25.9%** (56)
neurology	**22.7%** (49)
gynaecology	**7.4%** (16)
internal medicine	**6.5%** (14)
emergency	**0.9%** (2)
others	**0.9%** (2)
Amount Of Alerts [number of patients]	
1	**66.20%** (143)
2	**20.37%** (44)
3	**6.94%** (15)
4	**3.24%** (7)
5	**1.85%** (4)
6	**0.93%** (2)
7	**0.46%** (1)
eGFR Before Alert	
mean ± standard deviation [ml/min/1.73m²]	52 ± 22

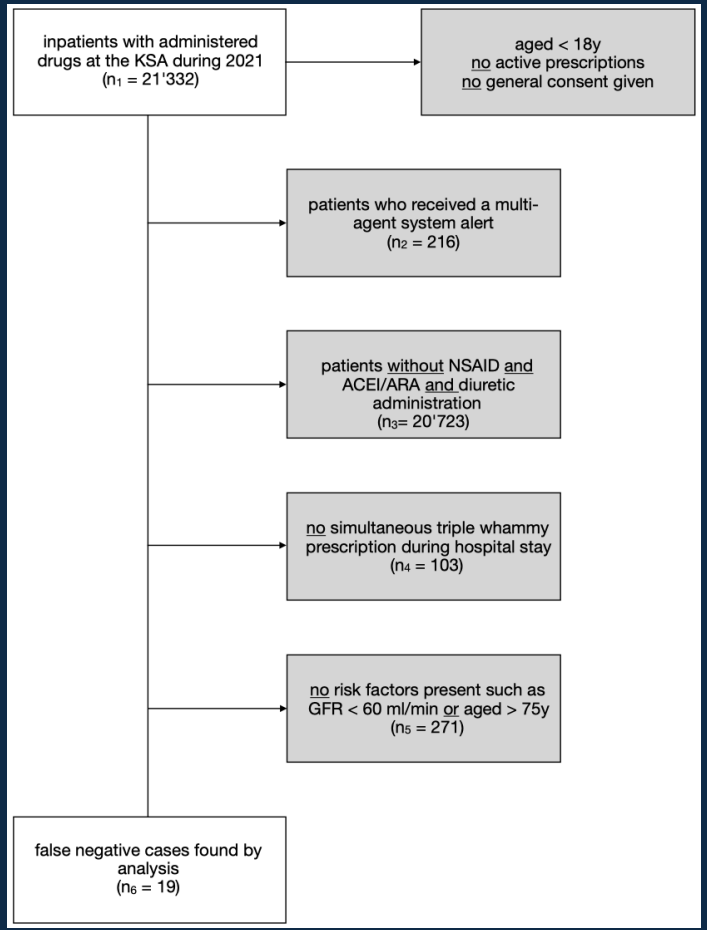
hospital ward	included wards
internal medicine	general internal medicine, angiology, dermatology, endocrinology, gastroenterology, oncology, infectiology, cardiology, nephrology, pneumology and rheumatology
surgery	plastic surgery, vascular surgery, ophthalmic clinic, otolaryngology, neurosurgery and urology
neurology	neurology
orthopaedics	orthopaedics wards and traumatology
gynaecology	breast centre, obstetrics ward and gynaecology
emergency	emergency

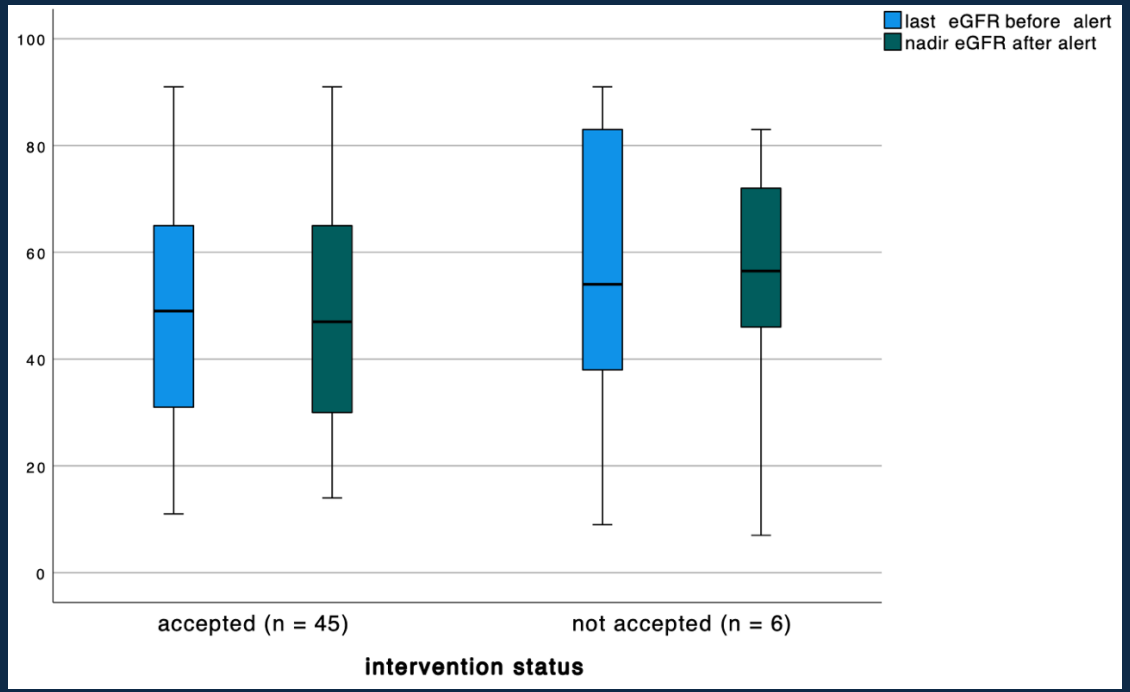
drug	ATC-Code
Amphotericin B	J02AA01
Ciclosporin	L04AD01
Tacrolimus	L04AD02
Vancomycin	J01XA01
Gentamicin	J01GB03
Tobramycin	J01GB01
Cidofovir	J05AB12
Aciclovir	J05AB01
Foscarnet	J05AD01
Ganciclovir	J05AB06
Adefovir	J05AF08
Quinine	M09AA* P01BC*
Bisphosphonates	M05BA* M05BB*
iodinated contrast media	V08A*
Digoxin	C01AA*
Aliskiren	C09XA02/53/52/54
Enoxaparin	B01AB05
Metformin	A10BA02, A10BD17/13/16/15/20/23/22/18/11/26/05/14/03/10/07/02/08/27/25
Lithium	N05AN01
Cisplatin	L01XA01
Carmustine	L01AD01
Semustine	L01AD03
Gemcitabine	L01BC05
Interferons	L03AB*
Methotrexate	L01BA01 L04AX03
Mitomycin	L01DC03

Drug	ATC-Codes	amount	percentage
Non-Steroidal Anti-Inflammatory Drugs (total = 346)			
Ibuprofen	M01AE01	184	53.2%
Diclofenac	M01AB05	98	28.3%
Acemetacin	M01AB11	19	5.5%
Etodolac	M01AB08	11	3.2%
Celecoxib	M01AH01	11	3.2%
Naproxen	M01AE02/52	11	3.2%
Etoricoxib	M01AH05	8	2.3%
Mefenamic Acid	M01AG01	2	0.6%
Ketorolac	M01AB15	1	0.3%
Nimesulide	M01AX17	1	0.3%
Diuretics (total = 282)			
Torasemide	C03CA04	157	55.7%
Hydrochlorothiazide	C03AA03/EA01	46	16.3%
Furosemide	C03CA01	44	15.6%
Spironolactone	C03DA01	21	7.4%
Indapamide	C03BA11	9	3.2%
Metolazone	C03BA08	3	1.1%
Chlortalidone	C03BA04	2	0.7%
Angiotensin-Converting Enzyme Inhibitor or **Sartan** (total = 382)			
Perindopril	C09AA04/BA04/BX01	91	23.8%
Lisinopril	C09AA03/BA03	85	22.3%
Valsartan	C09DA03/DB01/CA03/DX01/DX04	64	16.8%
Candesartan	C09DA06/CA06	53	13.9%
Olmesartan	C09DA08/CA08/DB02/DX03	30	7.9%
Irbesartan	C09DA04/CA04	19	5%
Losartan	C09DA01/CA01	17	4.5%
Telmisartan	C09DA07/DB04	9	2.4%
Ramipril	C09AA05	9	2.4%
Azilsartan	C09CA09	3	0.8%
Enalapril	C09AA02/BB02	2	0.6%


MAS-alert generated?
yes
message
true positive
patient dismissed
message required?
true positive
yes
false positive
no
termination by system
true positive
wrong or irrelevant
false positive
paused
false positive
no
detected by analysis?
yes
false negative
no
true negative


Triple Whammy alerts during 2021
343
intervention
paused < 15d
patient already dismissed
wrong or irrelevant
termination by system
124
4
85
accepted
73
not accepted
21
progression unknown
16
paused ≥ 15d
18
irrelevant
1
wrong
1


inpatients with administered drugs at the KSA during 2021 (n_1 = 21'332)
aged < 18y
no active prescriptions
no general consent given
patients who received a multi-agent system alert (n_2 = 216)
patients without NSAID and ACEI/ARA and diuretic administration (n_3= 20'723)
no simultaneous triple whammy prescription during hospital stay (n_4 = 103)
no risk factors present such as GFR < 60 ml/min or aged > 75y (n_5 = 271)
false negative cases found by analysis (n_6 = 19)


last eGFR before alert
nadir eGFR after alert
100
80
60
40
20
0
accepted (n = 45)
not accepted (n = 6)
intervention status