UNIVERSITEIT GENT

FACULTEIT GENEESKUNDE EN GEZONDHEIDSWETENSCHAPPEN

Triage en opnamebeleid

Update "Acute Intoxicaties"

Meet the Experts

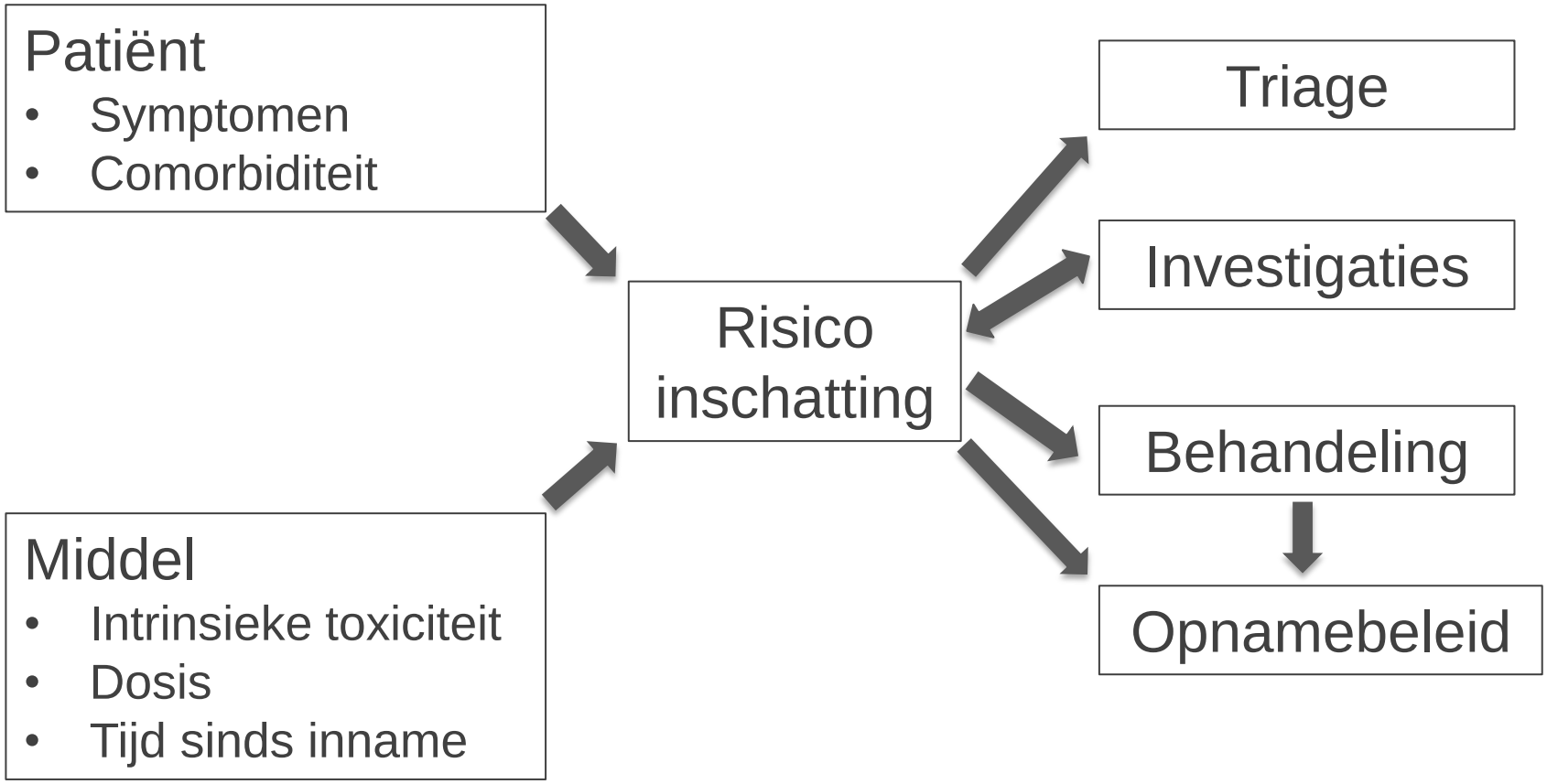
2de Lage Landen Symposium Intoxicaties

Vrijdag 13 september 2013

Peter De Paepe
Spoedgevallendienst UZ Gent
Heymans Instituut voor Farmacologie

Algemene aanpak van intoxicaties

- Resuscitatie
- Risico inschatting
- Supportieve therapie en monitoring
- Investigaties
- Decontaminatie
- Bevorderen eliminatie
- Antidoten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Middel
• Intrinsieke toxiciteit
• Dosis
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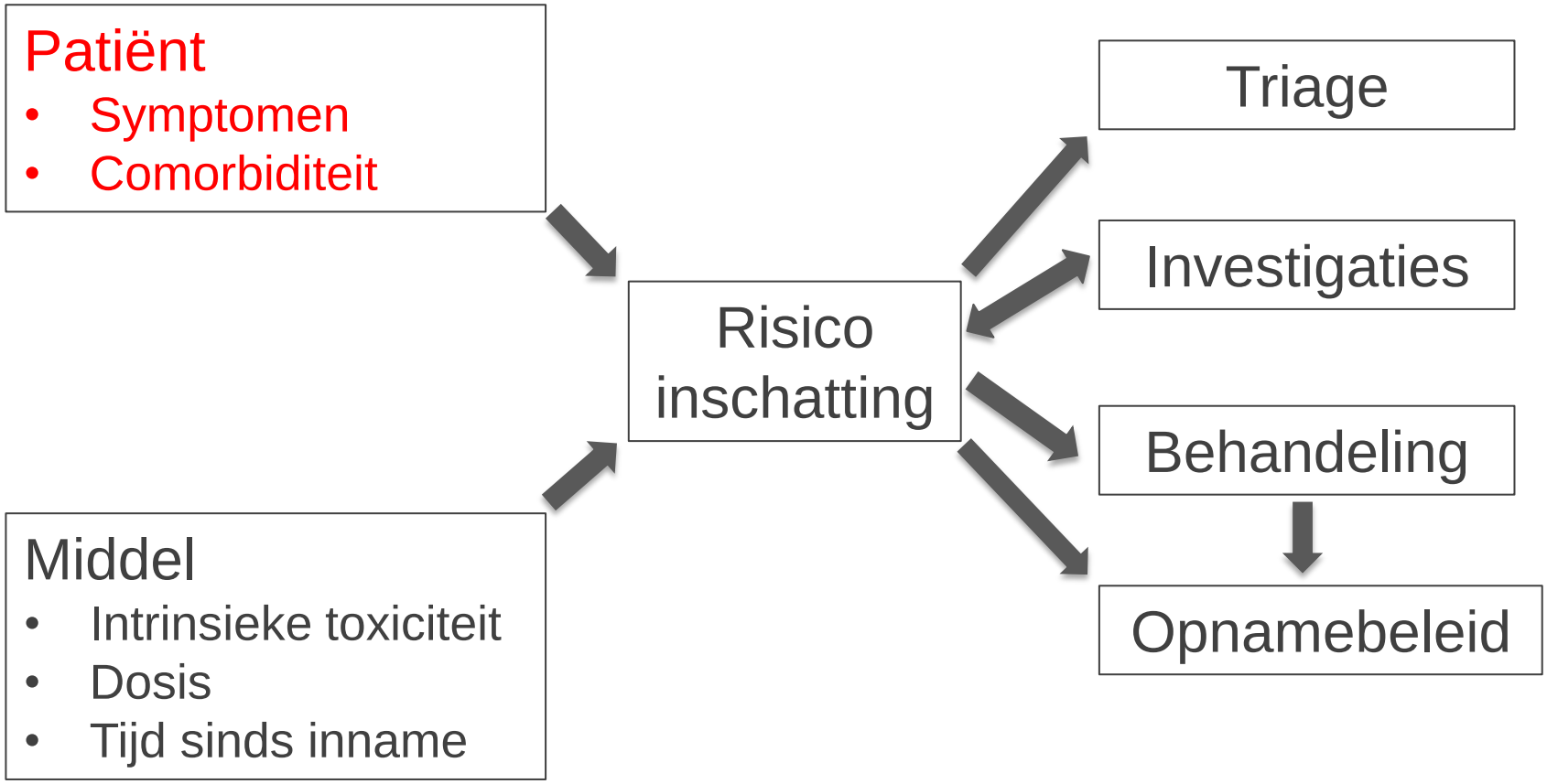
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Risico inschatting: de patiënt

Symptomen

- Vitale parameters – ABCDE
- Snel klinisch onderzoek
- Toxidromen

Comorbiditeit

- Snelle (hetero)anamnese
- Suïcidaliteit

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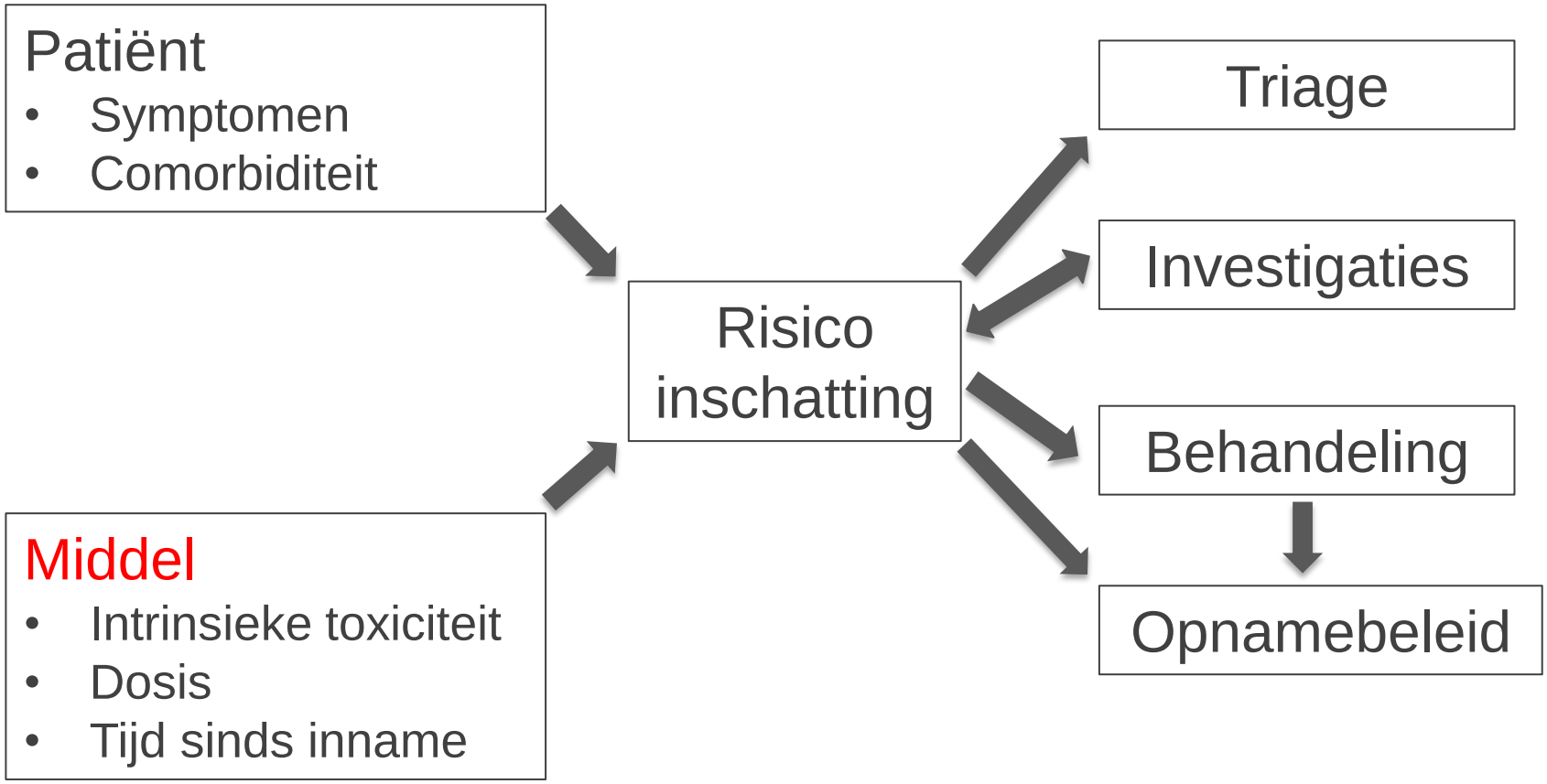
Hospital mortality among poisoned patients presenting unconscious

SUNE FORSBERG[1,4], JONAS HÖJER[2,4], and ULF LUDWIGS[3,4]

Degree of CNS-depression	Number of patients	Mean age (years)	Mean S-ethanol on admission	Hospital mortality rate
GCS score 3–6	444 (58%)	41.6	58.6 mmol/L ($n = 265$) (270 mg/dL)	4.3% ($n = 19$)
GCS score 7–10	327 (42%)	42.2	52.8 mmol/L ($n = 196$) (243 mg/dL)	0.3% ($n = 1$)

GCS = Glasgow coma scale.

Clinical Toxicology (2012), **50,** 254–257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Risico inschatting: het middel

- Literatuur
  - >> case reports, observationele studies
  - Retrospectief >> Prospectief
- Toxicokinetiek ≠ Farmacokinetiek
- Toxicodynamiek ≠ Farmacodynamiek
- Laattijdige-verlengde symptomen
  - Toxische tijdbommen
  - Preparaten met vertraagde vrijstelling
  - Bezoar
- Rol van het antigifcentrum

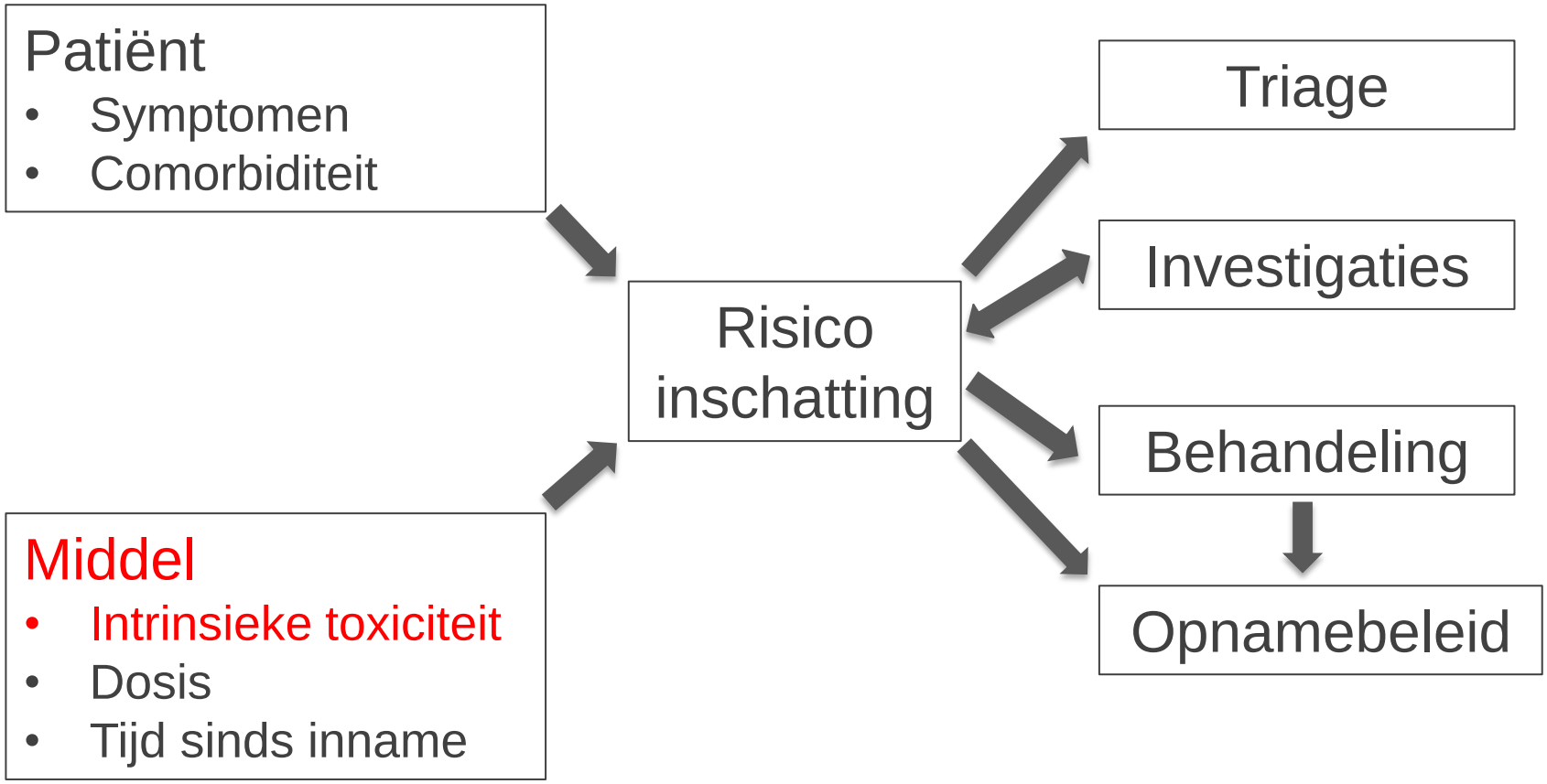
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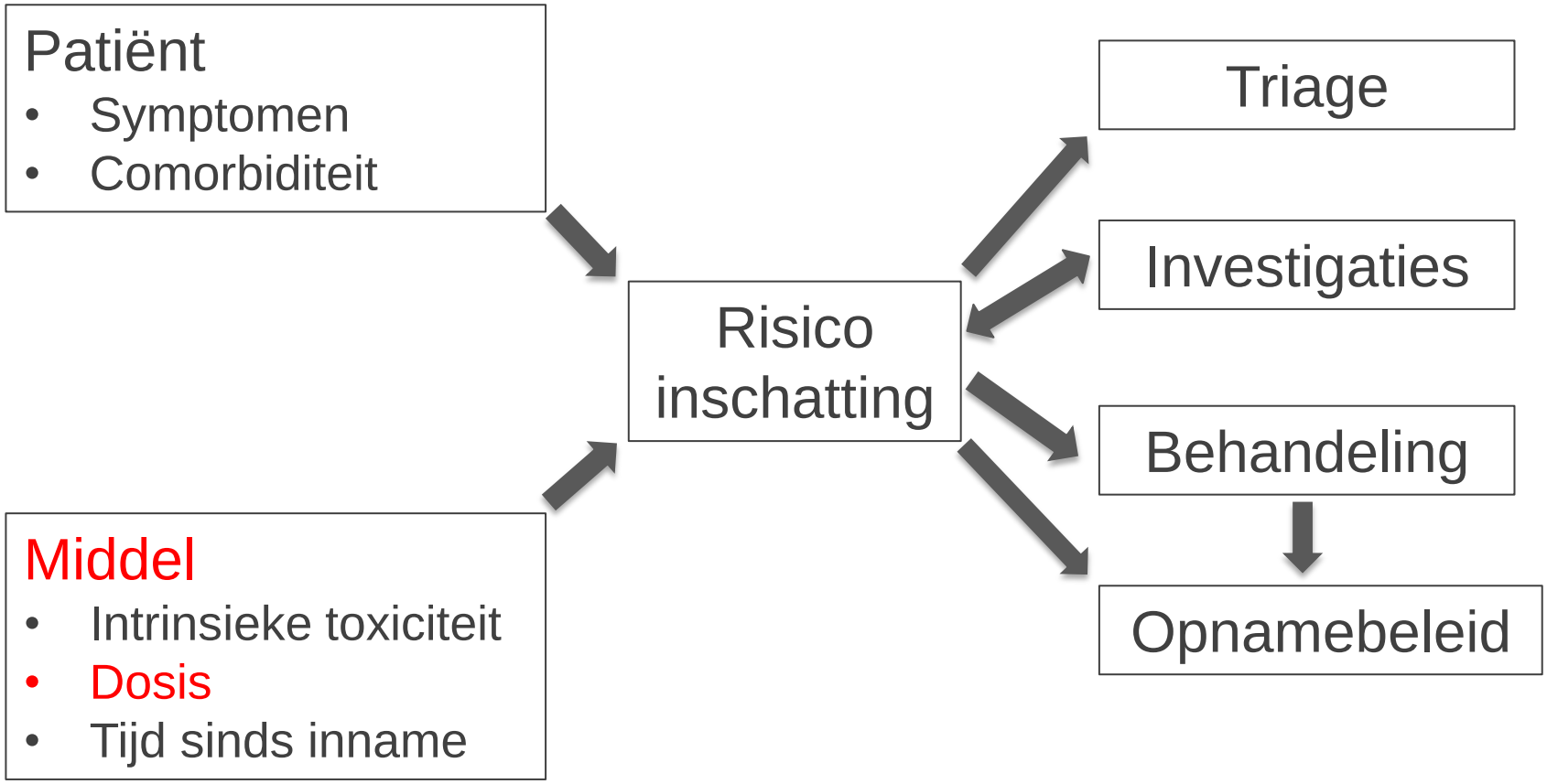
Table 18. Categories associated with largest number of fatalities (Top 25).[a]

Substance (Minor Generic Category)	All substances	%[b]	Single substance exposures	%[c]
Miscellaneous Sedative/Hypnotics/Antipsychotics	401	14.16	16	3.27
Miscellaneous Cardiovascular Drugs	305	10.77	53	10.84
Opioids	249	8.80	29	5.93
Miscellaneous Antidepressants	229	8.09	9	1.84
Acetaminophen Combinations	183	6.46	39	7.98
Miscellaneous Stimulants and Street Drugs	169	5.97	41	8.38
Acetaminophen Alone	162	5.72	67	13.70
Miscellaneous Alcohols	147	5.19	13	2.66
Miscellaneous Anticonvulsants	88	3.11	2	0.41
Miscellaneous Muscle Relaxants	80	2.83	4	0.82
Miscellaneous Antihistamines	78	2.76	8	1.64
Cyclic Antidepressants	73	2.58	13	2.66
Acetylsalicylic Acid Alone	60	2.12	19	3.89
Miscellaneous Fumes/Gases/Vapors	51	1.80	31	6.34
Nonsteroidal Antiinflammatory Drugs	48	1.70	2	0.41
Miscellaneous Unknown Drug	46	1.62	14	2.86
Oral Hypoglycemic	44	1.55	8	1.64
Miscellaneous Chemicals	36	1.27	17	3.48
Miscellaneous Hormones and Hormone Antagonists	32	1.13	3	0.61
Miscellaneous Anticoagulants	25	0.88	7	1.43
Miscellaneous Hydrocarbons	23	0.81	17	3.48
Miscellaneous Diuretics	21	0.74	0	0.00
Antibiotics	20	0.71	2	0.41
Cannabinoids and Analogs	19	0.67	6	1.23
Other Miscellaneous Drugs	18	0.64	3	0.61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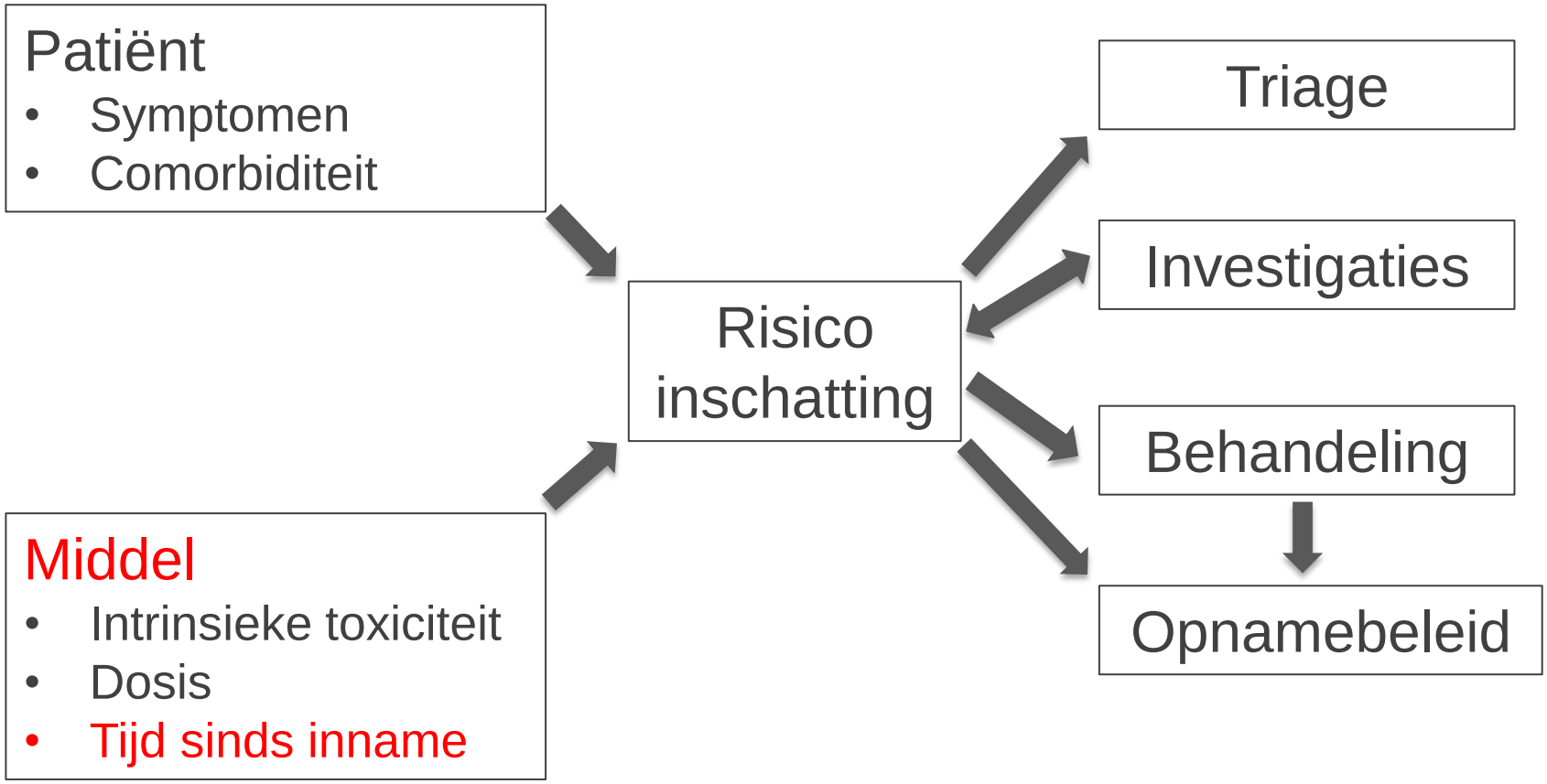
Doses resulting in severe cardiovascular failure
Acebutolol > 1.5 g
Carbamazepine > 10 g
Amitritptyline > 2 g
Chloroquine >4 g
Clomipramine >2 g
Dextropropoxyphen > 500 mg
Dosulepine > 1.25 g
Flecainide > 1.5 g
Maprotiline >3 g
Propranolol >2 g

Baud. Crit Care, 2007

Paracetamol: potentieel toxische dosis

Acute éénmalige inname

- > 150-200 mg/kg
- Indien risicofactoren: > 75 mg/kg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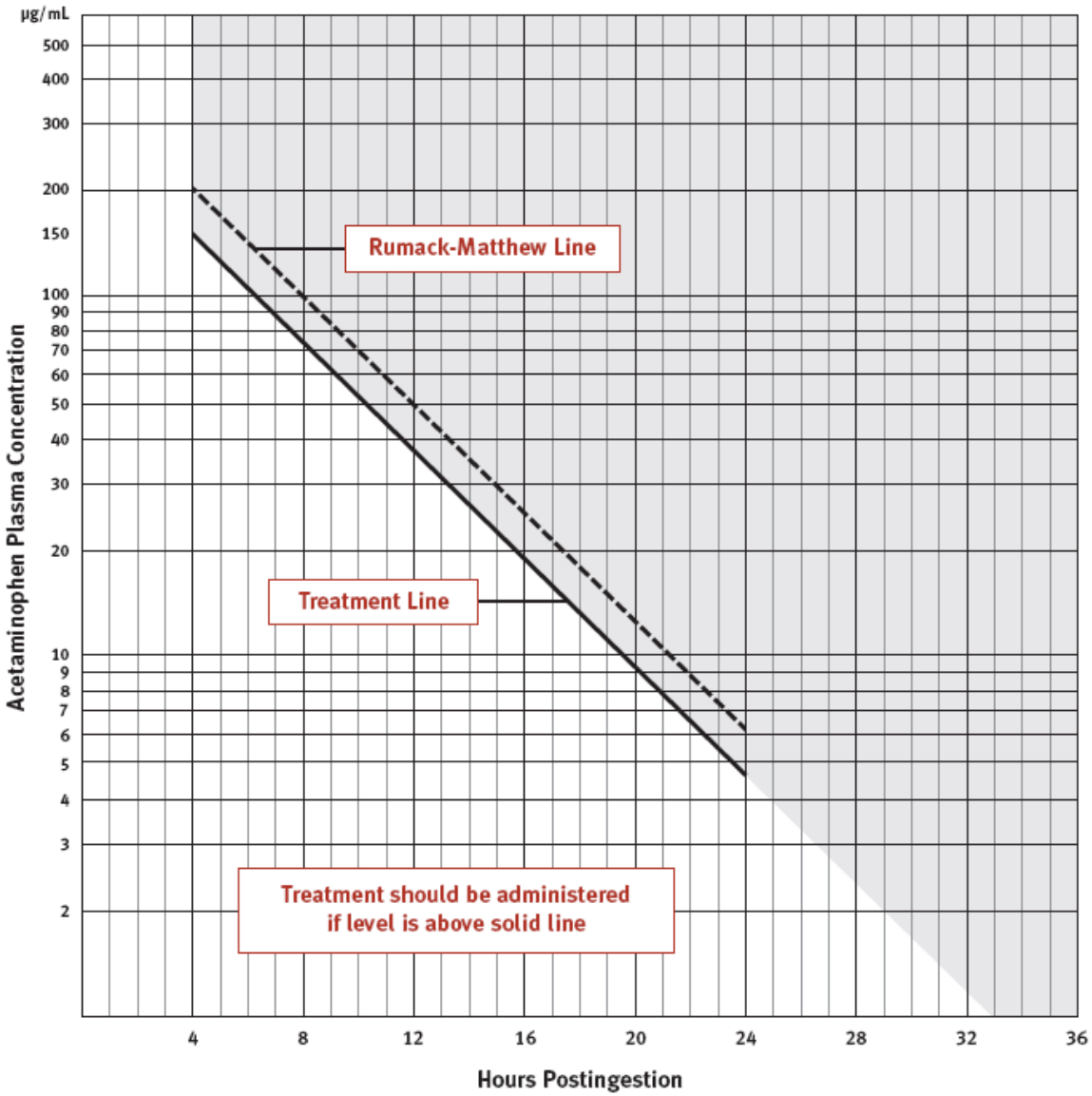


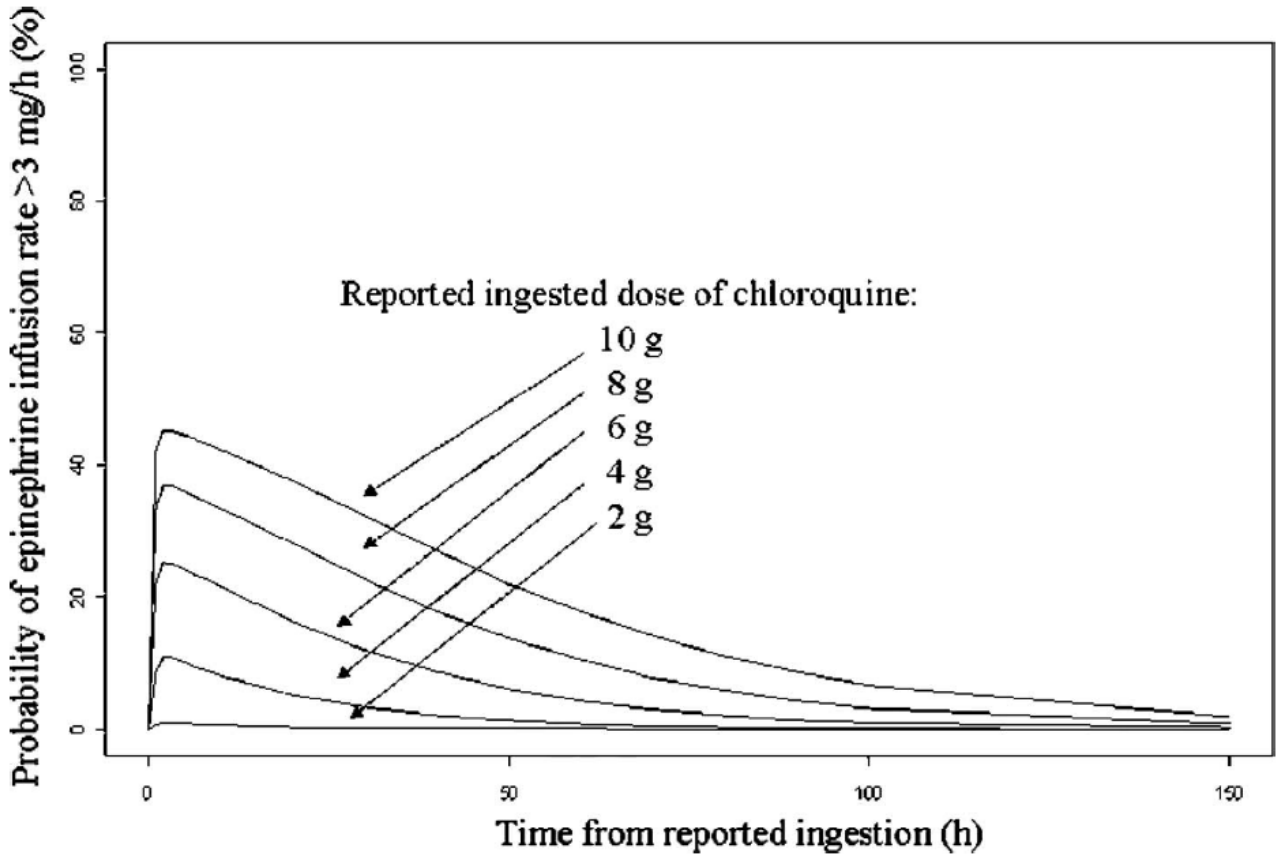
Nomogram: acetaminophen plasma concentration vs time after acetaminophen ingestion (adapted from reference 120, with permission). The nomogram has been developed to estimate the probability of whether a plasma acetaminophen concentration in relation to the interval postingestion will result in hepatotoxicity and, therefore, whether acetylcysteine therapy should be administered.

CAUTIONS FOR USE OF THIS CHART:

1. Time coordinates refer to time postingestion.
2. Graph relates only to plasma concentrations following a single, acute overdose ingestion.
3. The Treatment Line is plotted 25% below the Rumack-Matthew Line to allow for potential errors in plasma acetaminophen assays and estimated time from ingestion of an overdose.

For additional emergency information, call your regional poison control center. For special consultation, call the Rocky Mountain Poison and Drug Center toll-free number, 1-800-525-6115, available 24 hours a day.

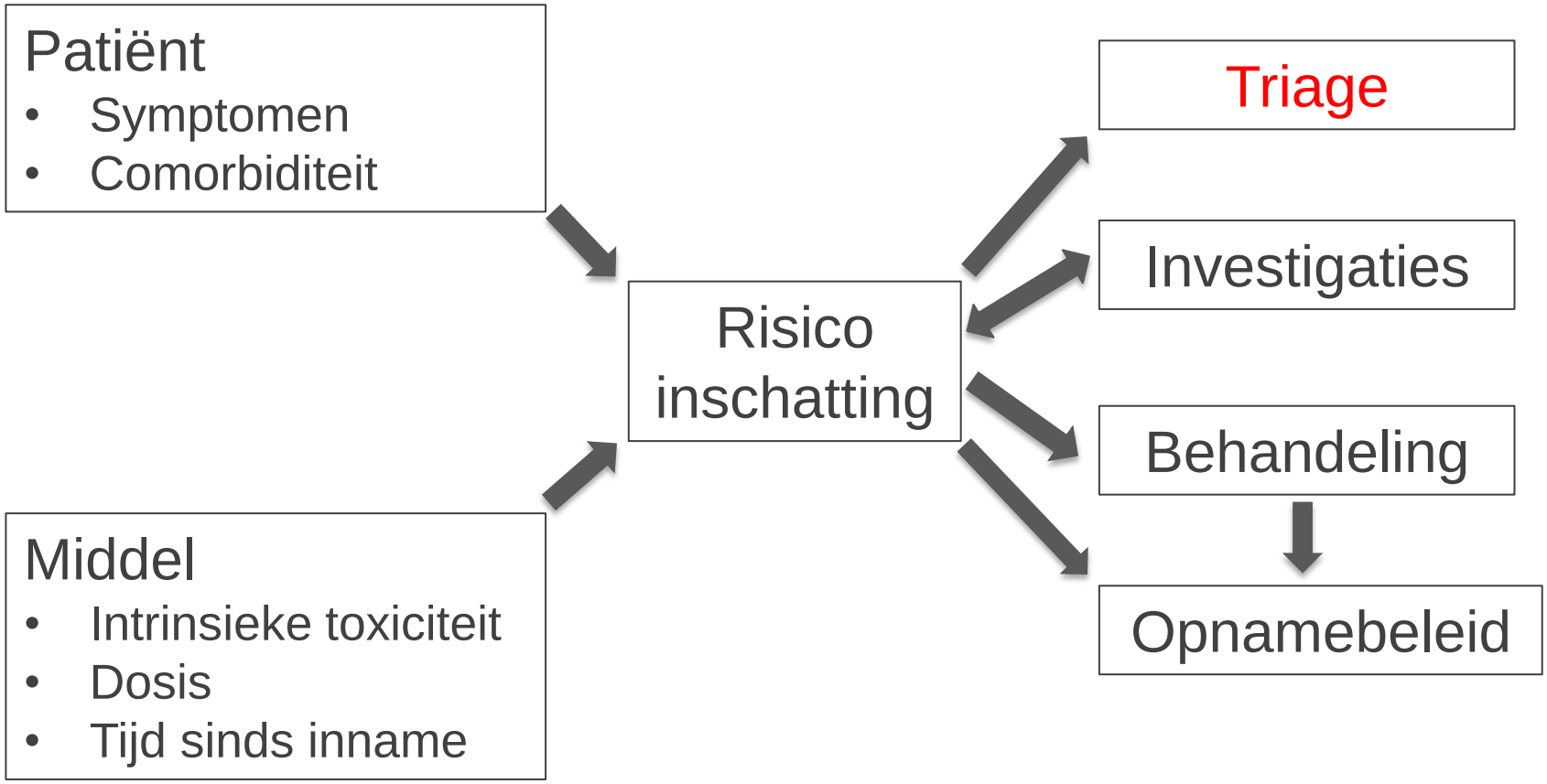
Epinephrine requirement based on the reported ingested dose in chloroquine poisoning: Usefulness and limitations of dose-effect modelling



Bruno Megarbane *Clinical Toxicology* (2011) **49**, 193–194

Risicostratificatie:
specifieke moeilijkheden bij intoxicaties

- Beperkte literatuurgegevens
- Frequent mengintoxicaties
- Beperkte kennis
- Patiëntgerelateerde factoren
  - Psychiatrische aandoeningen – suïcidaliteit
  - Bewustzijnsstoornissen
  - Beperkte/onbetrouwbare anamnese
  - Beperkte kennis van het ingenomen middel(en)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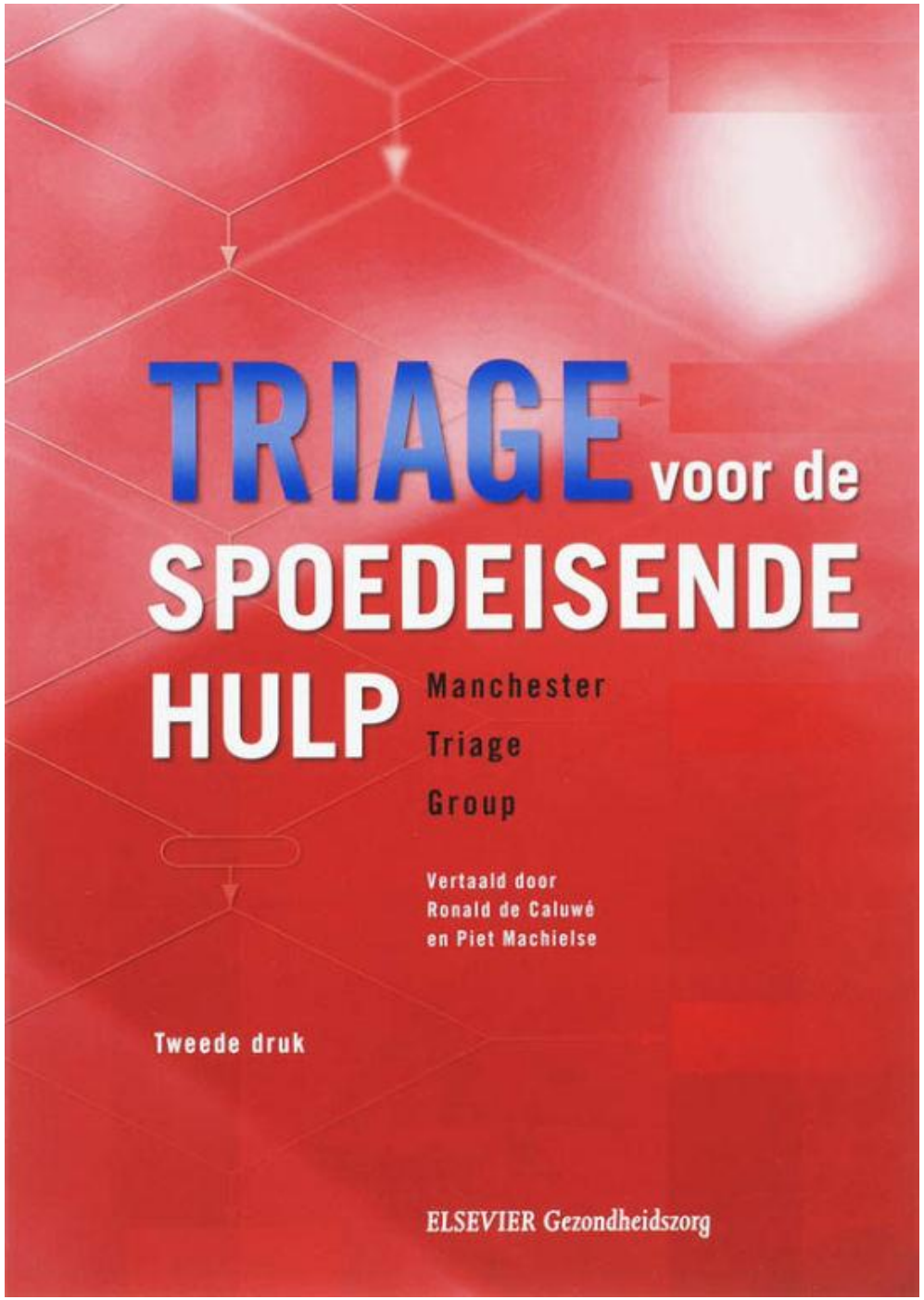
Triage en risicostratificatie

Triage System	Year	Countries
ATS: Australasian Triage Scale	1993	Australia, NZ
MTS: Manchester Triage Scale	1995	UK, ROI
CTAS: Canadian Triage & Acuity Scale	1997	Canada
ESI: Emergency Severity Index	1999	USA



Shock?
Inadequate breathing?
Airway compromised?
Definite danger to life?
Unresponsive GCS < 9?
Currently fitting?

⬇ N

GCS 9-12?
Systolic BP < 90 mmHg?
Overdose high lethality?
Probable threat to self or others?
Suicide/Homocide attempt?
Severe behavioural disturbance?
Abnormal pulse?
Cold <35°C?

⬇ N

Severe distress?
Overdose moderate lethality?
Possible danger to self or others?
Moderate to mild behaviour disturbance?
Perceptual disturbance?
Prolonged immobility?

⬇ N

Recent problem < 24hrs?
Semi-urgent mental health problem?
Moderate to mild behaviour disturbance?
Moderate to mild distress?

⬇ N

No or minimal distress?
Minor symptom of existing illness/injury
No risk discriminator identified

Triage en risicostratificatie: pitfalls

- Triagesystemen houden geen rekening met de specifieke toxiciteit of toxicokinetiek van het ingenomen middel
- Een stabiele patiënt sluit een ernstige intoxicatie NIET uit (“toxische tijdbommen”)
- Tijdsdruk
- Beperkte kennis van toxicologie

Iron Ingestion: an Evidence-Based Consensus Guideline for Out-of-Hospital Management

Atypical antipsychotic medicat

Dextromethorphan

An evidence-based consensus g

Selective serotonin reuptake inhibitor poison

for out-of-hospital managemen

based consensus guideline for out-of-h

β-Blocker Ingestion

Guideline for Out-of-Hospital Man

Ethylene Glycol Exposure: an E

Guideline for Out-of-Ho

Tricyclic antidepressant po

consensus guideline for o

Methylphenidate poisoning: A

guideline for out-of-hospital

Salicylate poisoning

of-hospital man

Valproic acid poi

Camphor Poisoning: An Evi

for Out-of-Hospital Manage

Acetaminophen Poisoning: an Evi

Guideline for Out-of-Hospital Management

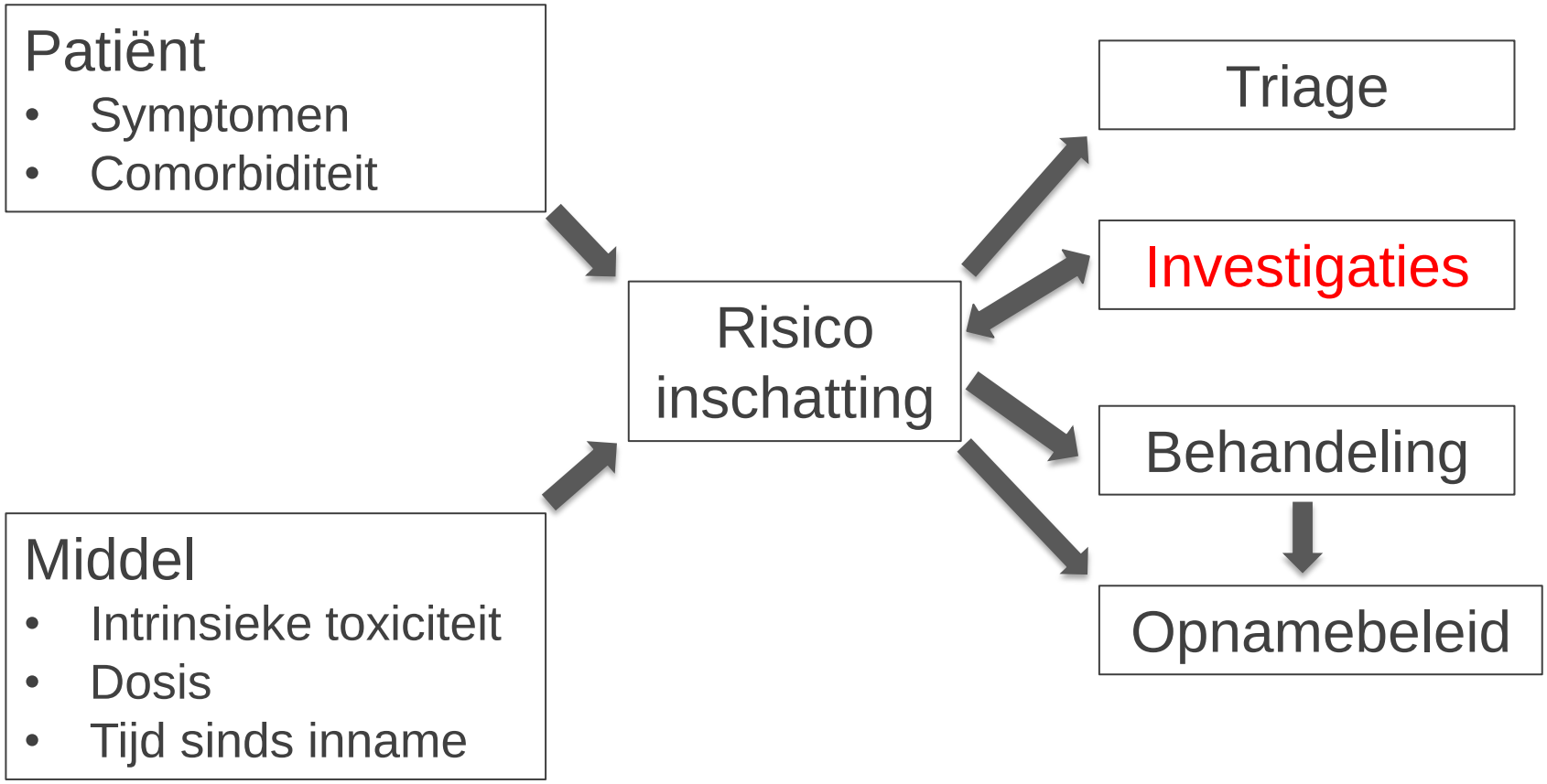
PRACTICE GUIDELINE

American Association of Poison Control Centers

Algorithm for triage of β-blocker ingestions

Is suicidal or malicious intent suspected?	YES → refer to emergency department.
NO ↓	
Is patient symptomatic? (e.g., weak, dizzy, syncopal)	YES → refer to emergency department.
NO ↓	
Have more than 6 hours (immediate-release preparation), 8 hours (sustained-release) or 12 hours (sotalol) passed since the ingestion?	YES → toxicity unlikely to occur. No referral or treatment is needed.
NO ↓	
Does patient have significant underlying cardiovascular disease, or is he/she taking a calcium channel blocker or another cardiodepressant drug?	YES → refer to emergency department or consult Medical Director.
NO ↓	
Is the home situation of concern? (e.g., patient lives alone or family/caregiver seems unreliable)	YES → refer to emergency department.
NO ↓	
Unable to estimate maximum amount ingested?	YES → refer to emergency department.
NO ↓	
Does maximum total possible dose exceed the referral threshold dose?	YES → refer to emergency department.
NO → Observe at home, periodic follow-up for 12-24 hrs	

Clinical Toxicology, 43:131–146, 2005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Risico inschatting en investigaties

- Electrocardiogram
- Arterieel bloedgas – Laktaat
- Labo
- Spiegels

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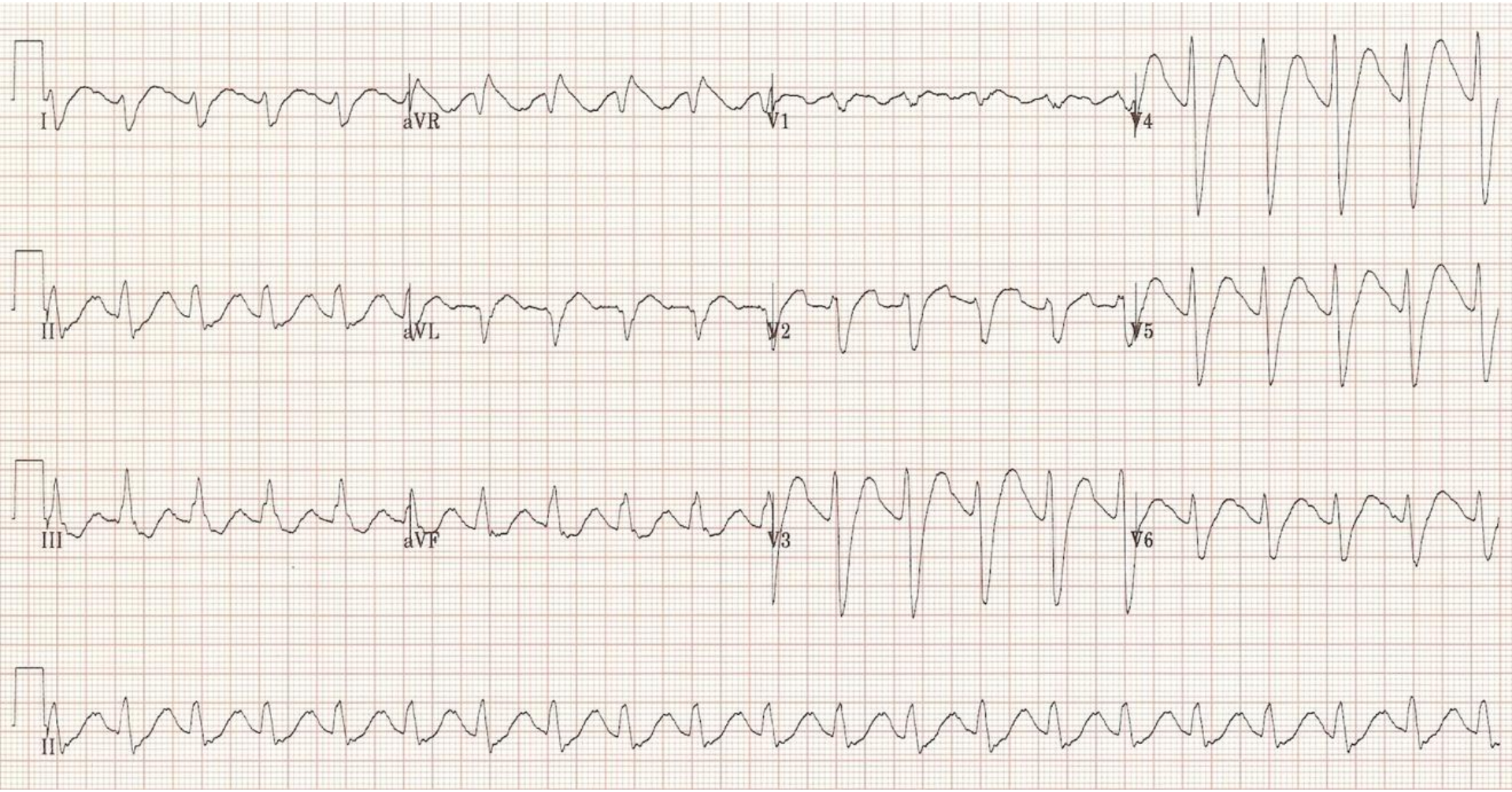


A Meta-Analysis of Prognostic Indicators to Predict Seizures, Arrhythmias or Death After Tricyclic Antidepressant Overdose[#]

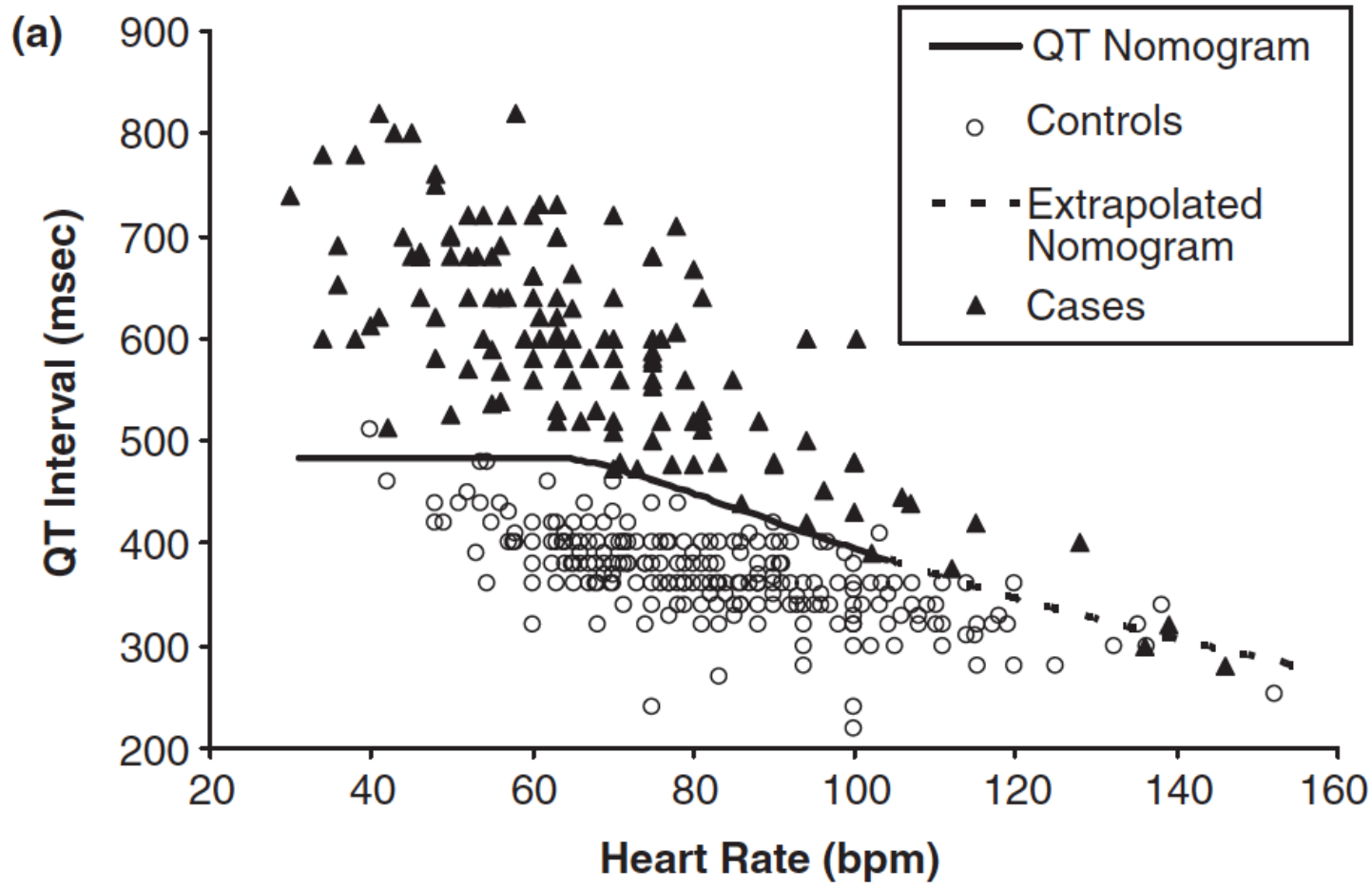
Benoit Bailey, M.D., M.Sc., F.R.C.P.C.,[1,2,*]
Nicholas A. Buckley, M.D., F.R.A.C.P.,[3]
and Devendra K. Amre, M.B.B.S., Ph.D.[2]

Criteria*	Number of studies/subjects included	Pooled sensitivity (95% CI)	Range sensitivity	Pooled specificity (95% CI)
QRS to predict death	5/599	0.81 (0.54–0.94)	0.75–1.0	0.62 (0.55–0.68)
QRS to predict seizures***	11/1334	0.69 (0.57–0.78)	0.44–1.0	0.69 (0.58–0.78)
QRS to predict ventricular arrhythmia	7/587	0.79 (0.58–0.91)	0.50–1.0	0.46 (0.35–0.59)

Journal of Toxicology
CLINICAL TOXICOLOGY
Vol. 42, No. 6, pp. 877–888, 2004

Drug-induced QT prolongation and torsades de pointes: evaluation of a QT nomogram

A. CHAN[1], G.K. ISBISTER[1,2], C.M.J. KIRKPATRICK[1] and S.B. DUFFUL[1,3]



Q J Med 2007; **100**:609–615

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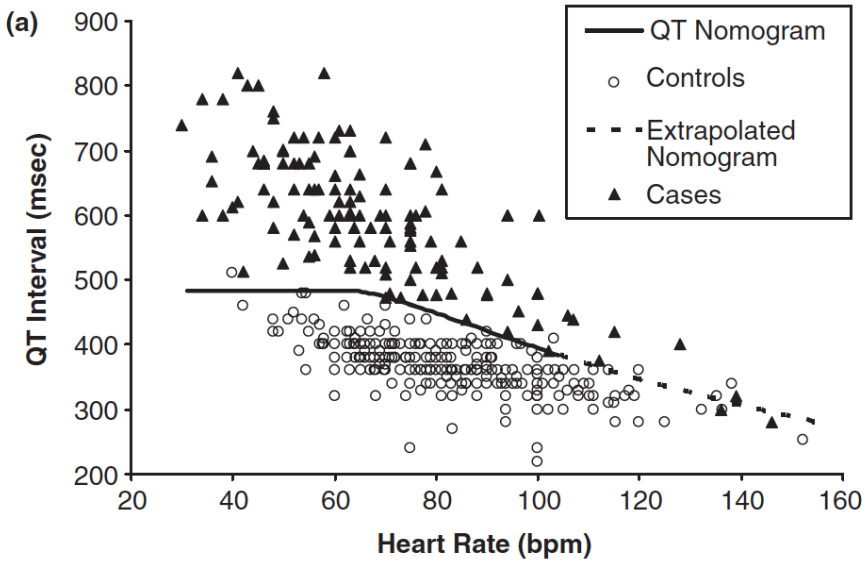
	QT nomogram (with extrapolation)	QT nomogram (no extrapolation)*
Sensitivity	96.9% (93.9–99.9)	98.3% (96.1–100)
Specificity	98.7% (96.8–100)	99.3% (97.8–100)



Q J Med 2007; **100**:609–615

Utility of serum lactate to predict drug-overdose fatality

ALEX F. MANINI[1], ASHISH KUMAR[2], DEAN OLSEN[3], DAVID VLAHOV[4], and ROBERT S. HOFFMAN[5]

Lactate cutpoint	Sensitivity % (CI)	Specificity % (CI)	NPV % (CI)	PPV % (CI)
HL*	90 (82–98)	66 (57–75)	93 (87–99)	57 (46–68)
>3.0	84 (74–94)	75 (66–84)	90 (84–97)	63 (51–75)
>4.0	72 (60–85)	88 (82–95)	86 (79–93)	75 (63–87)
>5.0	68 (55–81)	93 (88–98)	85 (78–92)	83 (71–95)

CI, confidence intervals; HL, hyperlactatemia; NPV, negative predictive value; PPV, positive predictive value.

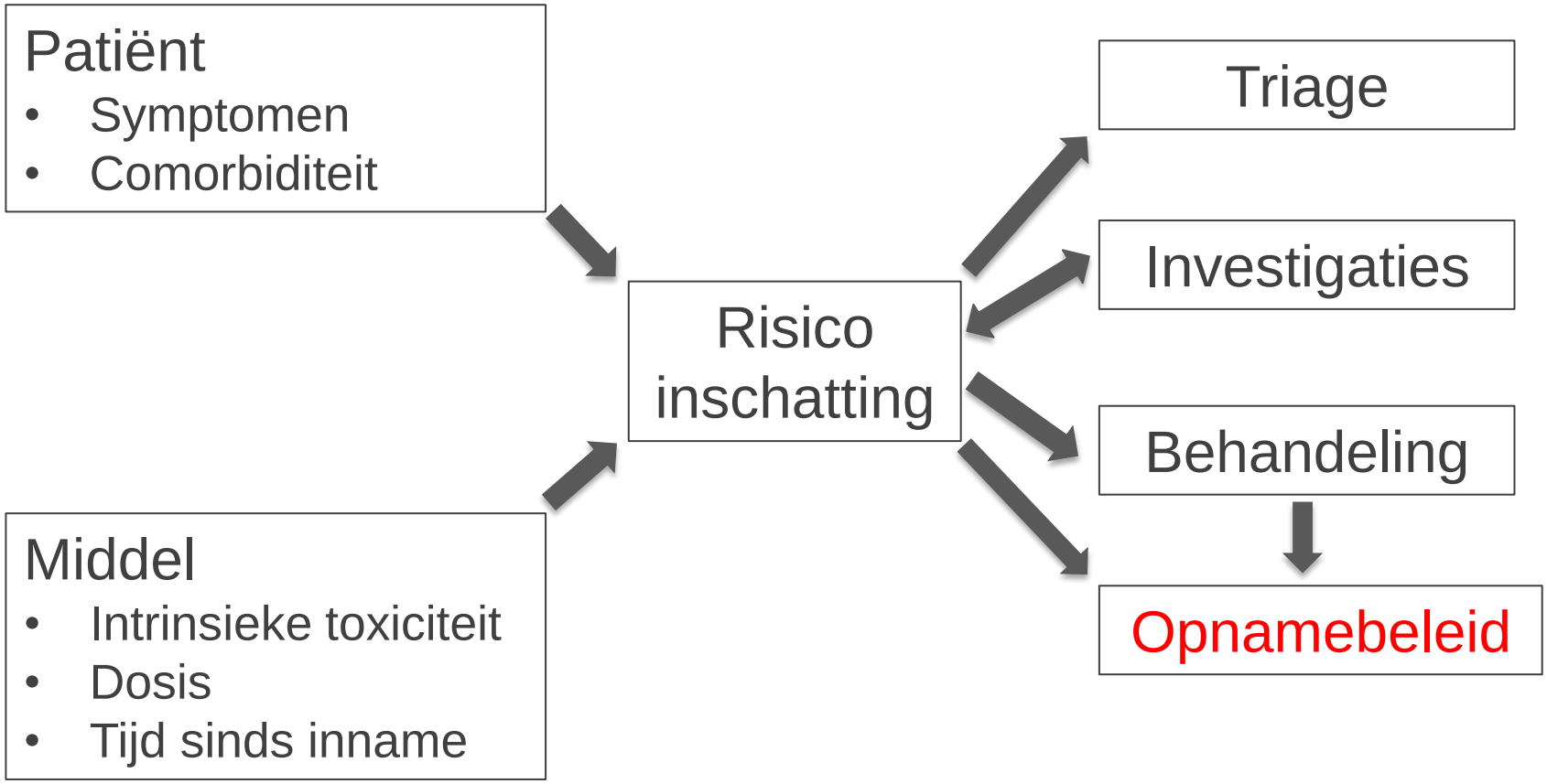
*Hyperlactatemia from assay defined per manufacturer as lactate concentration >2.5 mmol/L.

Clinical Toxicology (2010) **48**, 730–736

Toxicologische testen

Kwantitatieve analyse kan nuttig zijn voor o.a.

Anti-epileptica: carbamazepine, fenytoïne, valproaat	Methanol
Carboxyhemoglobine	Methemoglobine
Digoxine	Paracetamol
Ethyleenglycol	Paraquat
Zware metalen: ijzer, lood, kwik	Salicylaten
Lithium	Theofylline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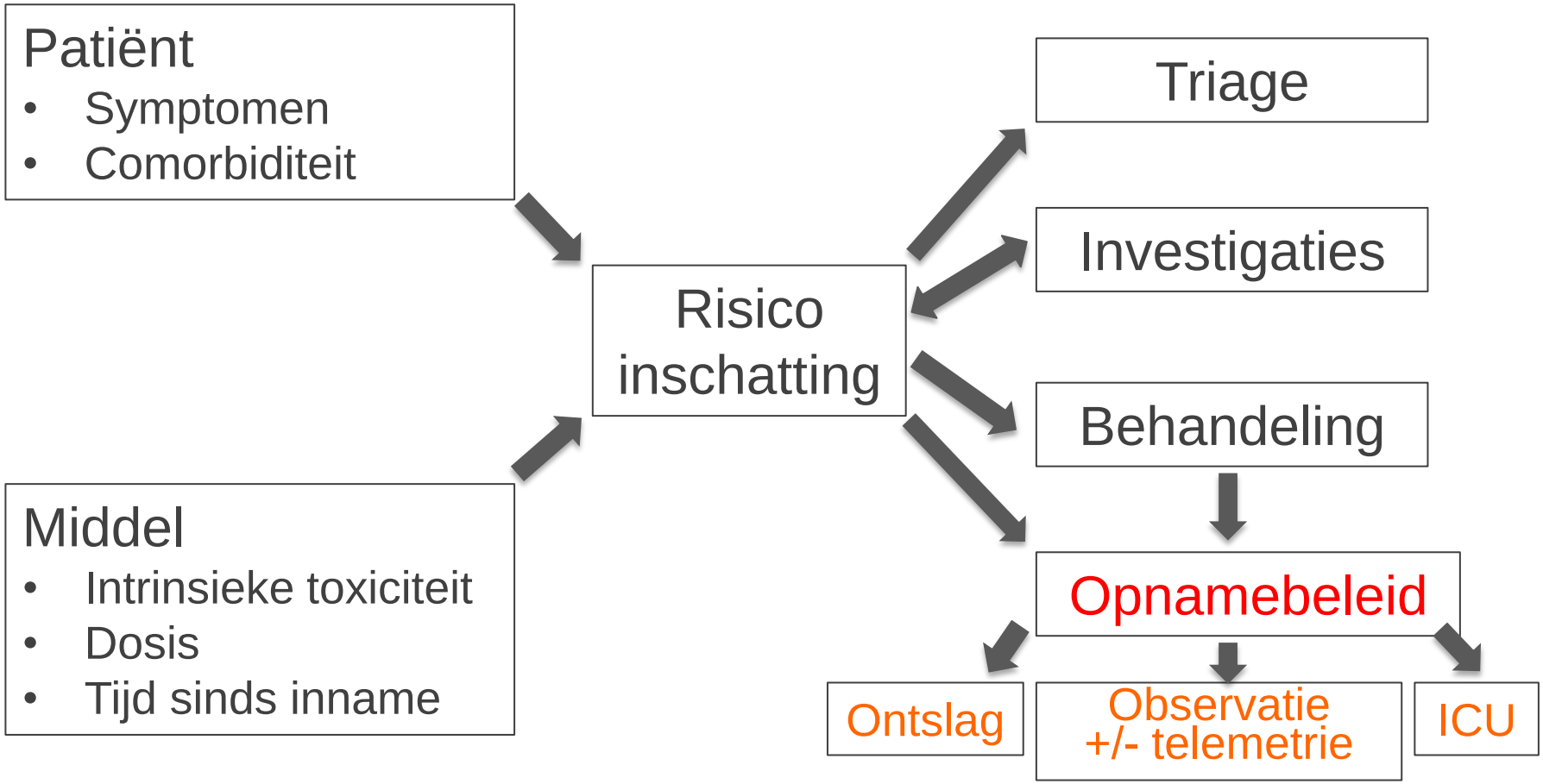
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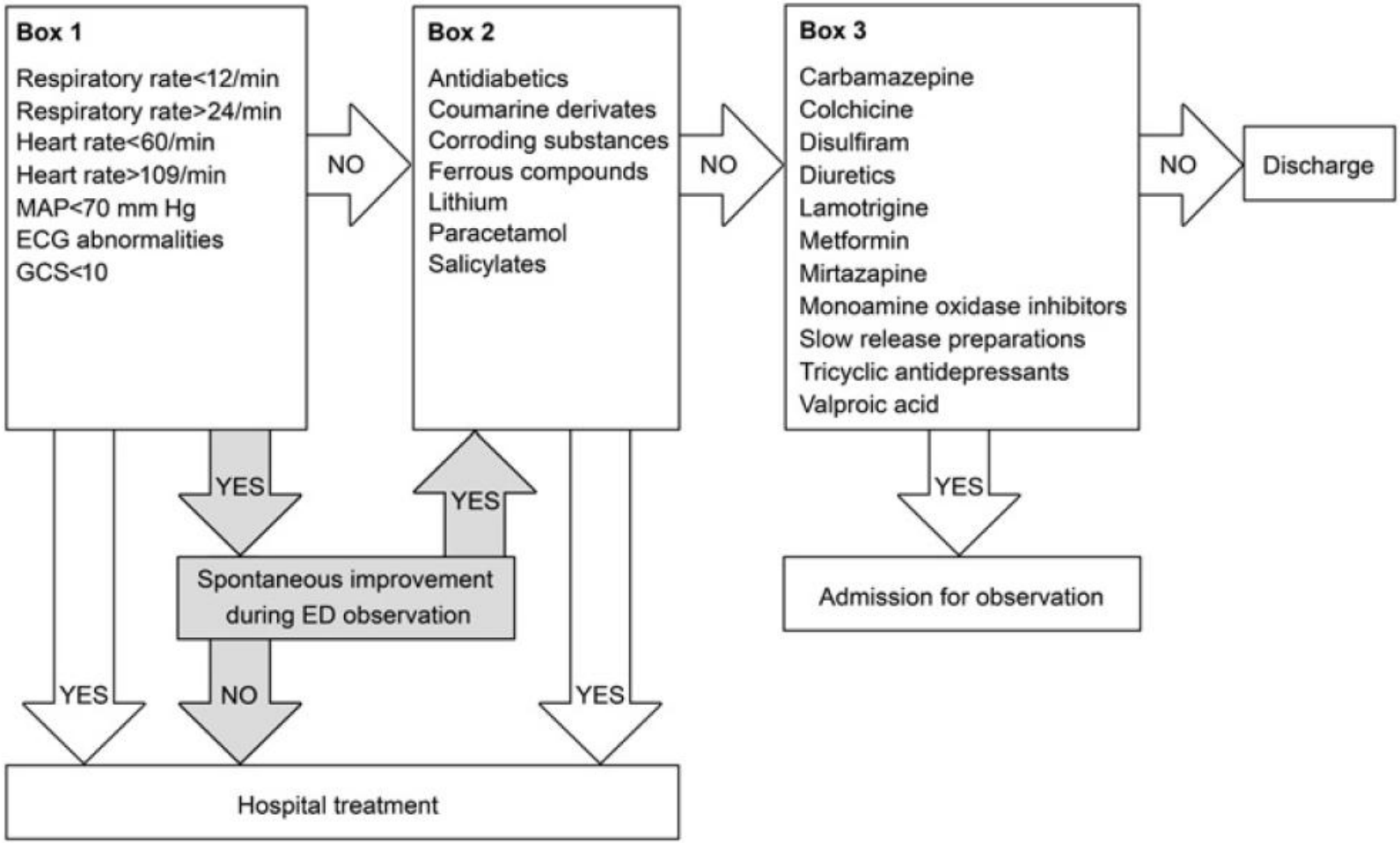
Ontslag
Observatie +/- telemetrie
ICU

2011 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 29th Annual Report

Site of management	N	%
Managed on site, nonhealth care facility	1,630,953	69.9
Managed in healthcare facility		
Treated/evaluated and released	295,110	12.6
Admitted to critical care unit	101,175	4.3
Patient lost to follow-up/left AMA	96,812	4.2
Admitted to noncritical care unit	65,845	2.8
Admitted to psychiatric facility	56,927	2.4
Subtotal (managed in HCF)	**615,869**	**26.4**
Other	28,708	1.2
Refused referral	40,316	1.7
Unknown	18,158	0.8
Total	**2,334,004**	**100.0**

Acute intoxication patients presenting to an emergency department in the Netherlands: admit or not? Prospective testing of two algorithms

R G A Ambrosius,[1] M P Vroegop,[2] F G A Jansman,[3] C W Hoedemaekers,[4] R E Aarnoutse,[5] G J van der Wilt,[6] C Kramers[1]



Emerg Med J 2012;**29**:467–472. doi:10.1136/emj.2010.106500

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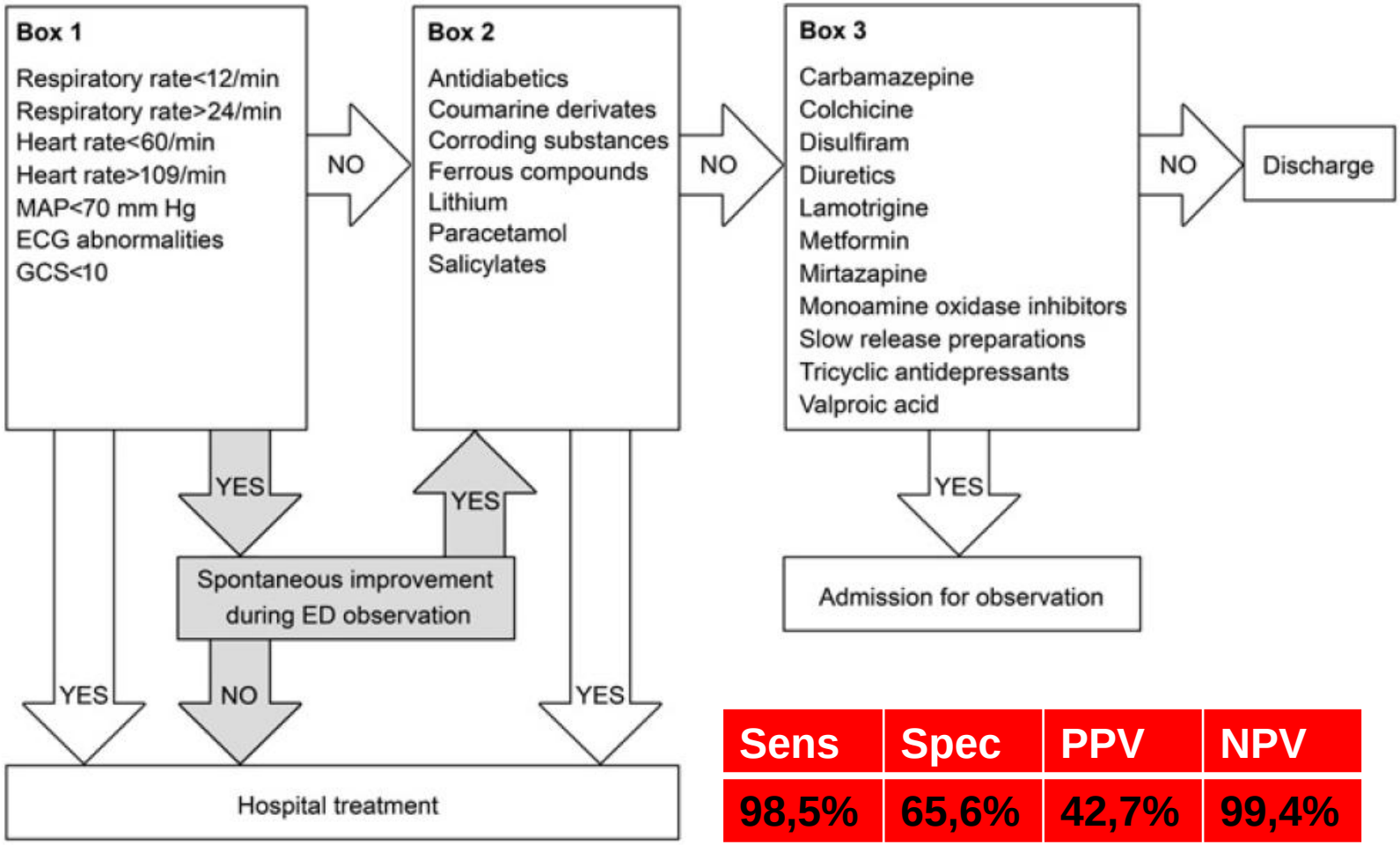

Sens	Spec	PPV	NPV
98,5%	65,6%	42,7%	99,4%

Emerg Med J 2012;**29**:467–472. doi:10.1136/emj.2010.106500

Indicaties voor ICU opname

- Levensbedreigende complicaties
- Specifieke behandeling
- Intensieve supportieve therapie
- Intensieve monitoring o.w.v.
  - Potentieel ernstige toxiciteit
  - Comorbiditeit

Intensieve monitoring: vereisten

- Voldoende bestaffing
- Voldoende ervaring
- Veilige omgeving voor suïcidale patiënt
- Veilige omgeving voor fysieke immobilisatie

Prognostische modellen voor ICU nood

- Acute Physiologic and Chronic Health Evaluation (APACHE) system
- Simplified Acute Physiologic Score (SAPS)
- Mortality Prediction Model (MPM)
- Sequential Organ Failure Assessment score (SOFA)
- Pediatric Risk of Mortality (PRISM)

➔ Meeste zijn gebaseerd op parameters tijdens de eerste 24u na ICU opname

➔ Onvoldoende gevalideerd voor intoxicaties

POISONING SEVERITY SCORE (PSS)
IPCS/EAPCCT

ORGAN	NONE	MINOR	MODERATE	SEVERE	FATAL
	0	1	2	3	4
	No symptoms or signs	Mild, transient and spontaneously resolving symptoms or signs	Pronounced or prolonged symptoms or signs	Severe or life-threatening symptoms or signs	Death
Cardio-vascular system		• Isolated extrasystoles • Mild and transient hypo/hypertension	• Sinus bradycardia (HR ~40-50 in adults, 60-80 in infants and children, 80-90 in neonates) • Sinus tachycardia (HR ~140-180 in adults, 160-190 in infants and children, 160-200 in neonates) • Frequent extrasystoles, atrial fibrillation/flutter, AV-block I-II, prolonged QRS and QTc-time, repolarization abnormalities • Myocardial ischaemia • More pronounced hypo/hypertension	• Severe sinus bradycardia (HR ~<40 in adults, <60 in infants and children, <80 in neonates) • Severe sinus tachycardia (HR ~>180 in adults, >190 in infants and children, >200 in neonates) • Life-threatening ventricular dysrythmias, AV block III, asystole • Myocardial infarction • Shock, hypertensive crisis	
Metabolic balance		• Mild acid-base disturbances (HCO_3 ~15-20 or 30-40 mmol/l; pH~7.25-7.32 or 7.50-7.59) • Mild electrolyte and fluid disturbances (K^+ 3.0-3.4 or 5.2-5.9 mmol/l) • Mild hypoglycaemia (~50-70 mg/dl or 2.8-3.9 mmol/l in adults) • Hyperthermia of short duration	• More pronounced acid-base disturbances (HCO_3 ~10-14 or >40 mmol/l; pH ~7.15-7.24 or 7.60-7.69) • More pronounced electrolyte and fluid disturbances (K^+ 2.5-2.9 or 6.0-6.9 mmol/l) • More pronounced hypoglycaemia (~30-50 mg/dl or 1.7-2.8 mmol/l in adults) • Hyperthermia of longer duration	• Severe acid-base disturbances (HCO_3 ~<10 mmol/l; pH ~<7.15 or >7.7) • Severe electrolyte and fluid disturbances (K^+ <2.5 or >7.0 mmol/l) • Severe hypoglycaemia (~<30 mg/dl or 1.7 mmol/l in adults) • Dangerous hypo- or hyperthermia	
Liver		• Minimal rise in serum enzymes (ASAT, ALAT ~2-5 x normal)	• Rise in serum enzymes (ASAT, ALAT ~5-50 x normal) but no diagnostic biochemical (e.g. ammonia, clotting factors) or clinical evidence of liver dysfunction	• Rise in serum enzymes (~>50 x normal) or biochemical (e.g. ammonia, clotting factors) or clinical evidence of liver failure	
Kidney		• Minimal proteinuria/haematuria	• Massive proteinuria/haematuria • Renal dysfunction (e.g. oliguria, polyuria, serum creatinine of ~200-500 µmol/l)	• Renal failure (e.g. anuria, serum creatinine of >500 µmol/l)	

' Persson H, Sjöberg G, Haines J, Pronczuk de Garbino J. Poisoning Severity Score: Grading of acute poisoning. J Toxicology - Clinical Toxicology (1998) 36:205-13.

Risk factors of developing serious toxicity needing ICU admission

- Unresponsiveness to verbal stimuli
- Seizures
- pCO2 > 45 mmHg
- Systolic BP < 80 mmHg
- QRS duration > 0.12 s
- Any cardiac rhythm (except sinus rhythm, sinus tachycardia, sinus bradycardia)

→ Retrospective analysis of 209 cases

no risk factor → N=151, none developed complications or required ICU admission

≥ 1 risk factor → N=58
- 35 required ICU intervention
- 7 developed high-risk complications

Brett et al. Arch Intern Med, 1987

Risicofactoren voor acute cardiovasculaire “events” (ACVE) bij patiënten opgenomen met een overdosis op de spoedgevallendienst

	ACVE N=82 (5.3%)	NO ACVE N=1475
Risk Factor:	OR (95% CI)	Adjusted OR* (95% CI)
QTc > 500 ms	25.7 (12.2-54.1)	27.6 (11.1-69.1)
Bicarbonate (<20 mEq/L)	10.7 (5.9-19.4)	4.4 (2.1-9.1)
Prior cardiac disease (CAD or CHF)	9.5 (5.6-16.4)	9.5 (4.9-18.4)

* Multivariable model also adjusted for: altered mental status, age, gender, and ED site.

Alex Manini, EAPCCT 2013, Copenhagen

Risicofactoren voor acute cardiovasculaire “events” (ACVE) bij patiënten opgenomen met een overdosis op de spoedgevallendienst

Risk Factors = (1) QTc > 500 ms, (2) Bicarbonate < 20, (3) Cardiac History

# Risk Factors	ACVE Rate (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	LR+ (95% CI)
Rule (≥1 Factor)	-	51.6 (41.1-62)	93.7 (92.4-94.8)	97.1 (96.2-97.9)	8.2 (6.3-10.7)
0 Factors	2.9% (2.0-3.7)				
1 Factor	27.2% (20.0-34.6)				
2+ Factors	90.9% (62.3-98.4)				

Alex Manini, EAPCCT 2013, Copenhagen

Conclusies

- Risico inschatting is essentieel voor vroegtijdige detectie van potentieel ernstige intoxicaties
- Consulteren van antigifcentra en andere informatiebronnen is cruciaal
- De huidige triagesystemen op spoedgevallen-diensten zijn onvoldoende specifiek
- Algoritmes en prognostische modellen m.b.t. complicaties en opnamebeleid zijn schaars en vaak onvoldoende gevalideerd