WHAT IS IN THE DRUG BOX?

- Gathering of Eagles
- June 2024
- James Augustine, MD
- Nick Simpson, MD
- Clayton Kazan, MD
- Michael Levy, MD
- Scott Gilmore, MD

WHERE ARE OUR MEDICINES? INSIGHTS ON DRUG SHORTAGES

- When – Never an Issue before 2010. Continuous Issue Since
- What – Critical Emergency Medications in Shortage
- Why – US Medication Producers
- How to Resolve – Federal Activity
- Workarounds

Drug	Shortage Status	Where Carried	Therapeutic Substitution	Management Plan
Acetaminophen	None		Ibuprofen	None needed
Adenosine	Some versions		Verapamil	Get state approval
Albuterol	Inhalers		Levalbuterol	Get state approval
Amiodarone	Some		Lidocaine	Substitute Lidocaine now, but leave on approval list
Aspirin	None		None	None needed
Ativan	Many		Midazolam, Valium	This is drug that needs refrig. Get state approval
Atropine	Many		None	Secure approval to tap hospital stocks
Calcium	Some versions		Other forms of calcium	Get state approval for all forms of calcium
Captopril	None		Lisinopril	Get state approval
Cardizem	None		Verapamil	Very limited use, not on most protocols. Get state approval.
Dextrose	Few		Different prep	Oral glucose
Dimenhydrinate	None		Diphenhydramine	Get state approval
Diphenhydramine	Many		Dramaine, Vistaril	Get state approval
Dopamine	Many		Dobutamine	None needed
Epinephrine	Many, including important 1:10,000		None	Need opportunity to tap hospitals, and have hospitals mix 1:10,000 vials
Etomidate	Many		Propofol (also short)	Get state approval
Fentanyl, Dilaudid	Many		Morphine and each other	Get state approval
Furosemide	None		Bumetanide	Get state approval
Glucagon	Many		None	Very expensive. Substitute glucose or IN D50
Glucose (oral)	None		None	None needed
Haloperidol	Many		Droperidol	Get state approval
Heparin	Few		Different version	None needed. Not an important EMS medicine
Hydroxocobalamin	None		Lilly Kit	Assure state approval
Ipatropium	None		Straight albuterol	None needed
Ketorolac	None		None	Get state approval
Lidocaine	None		Amiodarone	None needed
Magnesium	Many		Different version	Assure approval to tap hospital stocks
Metoprolol	Some		Other beta-blockers	Get state approval
Naloxone	Many		None	Assure approval to tap hospital stocks
Nitroglycerine	None		None	Assure approval to tap hospital stocks
Ondansetron	Acute		Promethazine	Get state approval
Promethazine	Many		Zofran, Compazine	Get state approval
Sodium Bicarbonate	None		None	None needed
Solumedrol	Many		Dexamethasone, hydrocortisone	Get state approval

EMS STRATEGIES 2011

Alternate Medications

Active Stock Management

Just in Time Education

Budget for Higher Prices

RECENT MANAGEMENT STRATEGIES

- ***Partnerships*** - Working with fellow regional healthcare providers
- ***Deployment***
  - Active stock management plan
  - Deployed "just in time"
  - Avoiding exposures of medicines to degradation
  - Reduce waste or diversion
- ***Substitute Oral Medications***
- ***Use of Expired Medications -*** Science says that many drugs maintain their potency past their manufacturer imposed expiration dates.
- ***Alternate Medicine Sources, Including Compounding***
  - Products like cardiac epi
  - Price for compounded medicines is 8 to 10 times more
  - Limited shelf life, on average being 6 months
  - New England Compounding Center in Framingham, MA in October 2012

IAP ELEMENTS FOR ED MED SHORTAGES

- Logistics
  - Supplies, Storage, Allocation
  - Communications with ED Nursing
  - Mutual Aid Exchanges
- Finance
  - Budgets
- Liaisons
  - Hospital Pharmacy and Medical Staff
  - Local Dept of Health
- Safety
  - Patient Safety Education
  - Local Pharmacy Interaction – Who has the Medication?

LEVEL 1 ADVISORY

Advisory and Preparatory Activities

Hospitals
Intel and Feedback on shortages
Design and approve agreements for sharing meds with each other and EMS

County EMS and Fire Agencies
Develop therapeutic equivalent list
Make appropriate protocol changes to allow substitutions
Using paramedic input design:
- Packaging solutions for safety
- Safety program
- Needed just in time educational programs

DOH
Assist in study of tracking program for typical and atypical meds
Study sources for atypical meds

Planning Team
Study legal and regulatory challenges and develop recommendations
Design medication tracking program and what elements of DOH program that can be applied
Create the process for declaring shortage and allowing compounding
Design a "no risk" safety reporting program
Study the central sourcing program
Publish "Drug Shortage Status Bulletin" for Command Team, state, local hospitals and providers
Develop LEVEL 3 elements and props

Finance
Budget projections on the impact of this program
Purchase Order process for timely and emergency acquisition, and designate a compounding pharmacy
Study reliable sourcing and pricing programs

LEVEL 2 MODERATE SHORTAGES

Medication shortages affect availability and patient care in emergency operations, with Life Threatening Risk

Trigger: When multiple therapeutic substitutions are being used, and multiple medicines are in shortage status at hospital and EMS sources

Hospitals approve agreements for sharing meds with each other and EMS

County EMS and Fire Agencies
Implement protocol changes to allow substitutions
Using paramedic input design initiate:
- Packaging solutions for safety
- Safety program
- Just in time educational programs

First stage of "Medication Command" utilization

DOH implements elements of tracking program for typical and atypical meds
Initiate sourcing for atypical meds

Planning Team
Implement needed legal and regulatory changes
Finalize state "releases"
Implement process for declaring shortage and start needed compounding program
Implement medication tracking program and elements of DOH program
Implement "no risk" safety reporting program
First stage implement central sourcing program
First stage of drug quality management program
Final design LEVEL 3 elements and props

Finance
Purchase Order process for timely and emergency acquisition

LEVEL 3 SEVERE SHORTAGES

Many medication shortages affect patient care, with Life Threatening Risks

Trigger: When many medicines are in therapeutic substitutions at hospital and EMS

Hospitals actively sharing meds with each other and EMS

County EMS and Fire Agencies
Implement protocol changes to allow substitutions
Implement:
Full complement of packaging solutions for safety
Safety program
Just in time educational programs
Uniform use of "Medication Command" program, with core group of designated personnel and distribution program

Make full use of DOH tracking program for typical and atypical meds
Implement program for use of atypical meds

Planning Team
Implement needed legal and regulatory changes
Declare shortage and fully utilize compounding program
Implement central medication sourcing program and elements of DOH program
Convert to drug quality management program doing active analysis of the "no risk" safety reporting program
Design the "all clear" criteria
Integrate Finance and timely emergency acquisition

Aftermath
Active medicine inventory management with overall less budget impact
Safer medicine packaging and "No Risk" rpting
Expanded protocols and JIT education program

WHAT DRUGS NEEDED IN EMS

Meds used nationally in a year
US EMS system with 36 million pts

	Approx Med doses
Saline	1,807,799
Ondansetron	741,835
Aspirin	703,388
Epinephrine	566,304
Naloxone	520,522
Albuterol	478,082
Fentanyl	485,623
Midazolam	188,733

- **Then**
- Nitroglycerin
- Ipratropium
- Methylprednisolone
- Dextrose
- Benadryl
- Droperidol
- Ketamine
- Magnesium sulfate
- Amiodarone
- Atropine
- Adenosine
- Bicarbonate

HOW TO RESOLVE?

- Monthly EMS Meetings w FDA not Working
- CivicaRX
- Mark Cuban
- This is a National Security Issue
- Defense Production Act
- US Senate Action

Senate Finance Committee Discussion Draft:
Preventing & Mitigating Generic Drug Shortages

Overview of the Problem

Shortages in the supply of prescription drugs present a persistent and growing challenge in the United States, resulting in worse outcomes and higher costs for patients and the health care system. This month, the American Society of HealthSystem Pharmacists (ASHP) announced that drug shortages have reached an all-time high—with 323 medicines now in short supply. Generic drugs comprise the majority of medications in shortage at any given time, and a recent analysis found that 56 percent of drugs in shortage in 2023 cost less than $1 per unit. Generic injectables have proven particularly vulnerable, representing an estimated 67 percent of shortages overall.

Summary of Discussion Draft

The Senate Finance Committee has developed bipartisan legislation to prevent and mitigate generic drug shortages across the U.S. using the power of the Medicare and Medicaid programs. Specifically, the Committee's draft proposal would: (1) establish new authority and resources within Medicare to reform provider (hospital and physician) purchasing of generic drugs at high risk of shortage; and (2) modify the Medicaid program to allow generic manufacturers to address economic challenges creating shortages for numerous retail drugs.

Beginning in 2027, a new **Medicare Drug Shortage Prevention and Mitigation Program** would leverage targeted provider payment incentives to promote improvements and reforms in contracting and purchasing practices across the supply chain that enhance resiliency, reliability, and sustainability, with a focus on generic drugs confronting high shortage risks, beginning with generic sterile injectables (such as saline used in hospital settings) and infused medications (such as chemotherapy), with the potential for expansion to additional multiple-source drugs over time. Under the voluntary program, with respect to participating providers, manufacturers, and other entities, the following requirements would apply:

Bringing up players from the Pharm Team

Nick Simpson, MD FACEP FAEMS

No financial disclosures

1. How could a Clinical PharmD help as an EMS medical director?

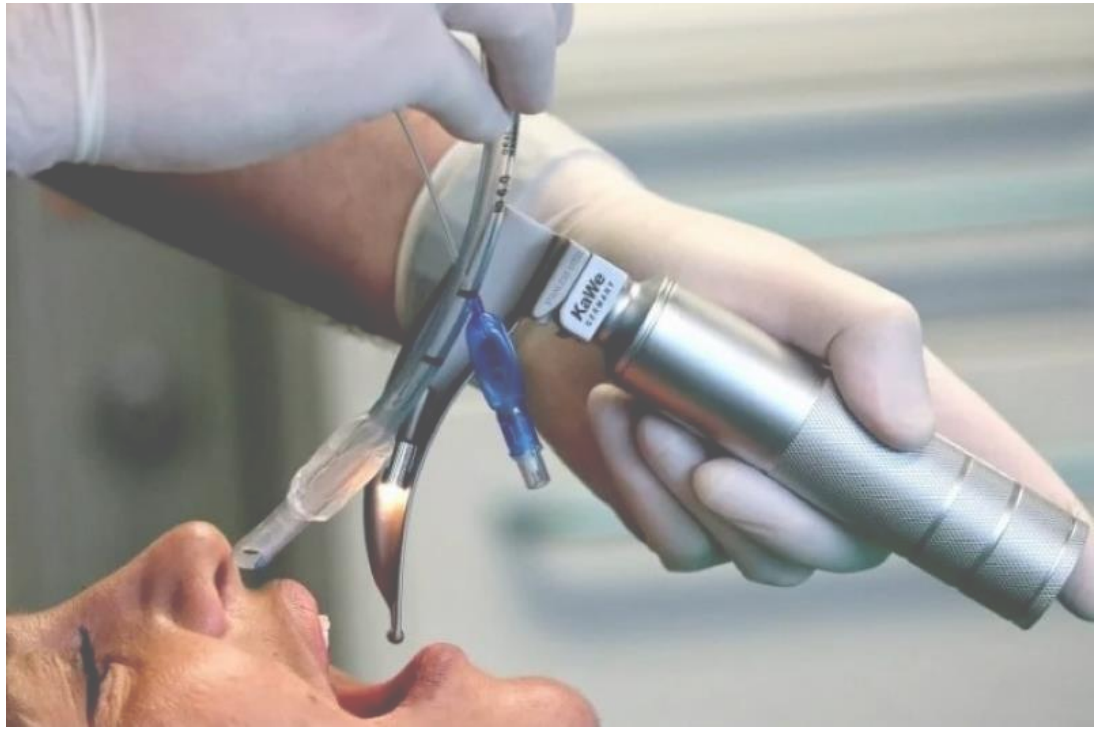
2. Why would anyone pay them for it?

Clinical PharmD can help with “RSI”

Review of protocols/meds

Shortage mitigation

Interfacing with Hospitals and Pharmacists



Review of Protocols / Meds

Continuous review of protocols with medical direction team

Evaluating new studies/literature

Creation of Medication reference sheets

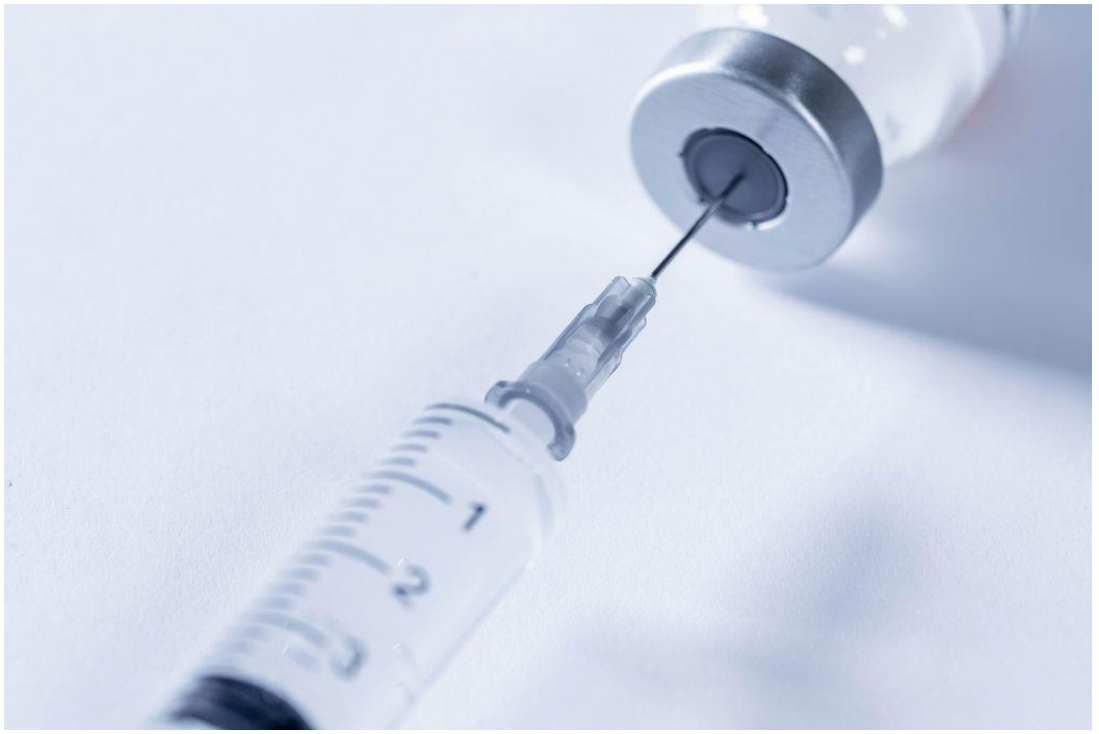
Understanding the logistics of storage, stability/shelf-life, & cost

A resource to the paramedics for questions/concerns

Drug **Shortage** Mitigation

Understands the WHOLE system

Health system medication supply re-distribution/advocacy



Interface with Hospitals/Pharmacists

Adds another layer to validity of EMS decisions made

Able to connect with Pharmacists in a different way

1. How could a Clinical PharmD help me as an EMS medical director?

2. Why would anyone pay them for it?

Clinical PharmD can help with “RSI”

Review of protocols/meds

Shortage mitigation

Interfacing with Hospitals and Pharmacists

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CeleCor Therapeutics

CeleBrate

Phase 3 prospective, blinded, randomized, placebo controlled, international multicenter study to assess the safety and efficacy of a single subcutaneous injection of zalunfiban in subjects with ST-elevation myocardial infarction in the pre-hospital setting

Michael Levy, M.D. FAEMS, FACEP, FACP

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Medical Director Anchorage Fire Department
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AFD Department Physician

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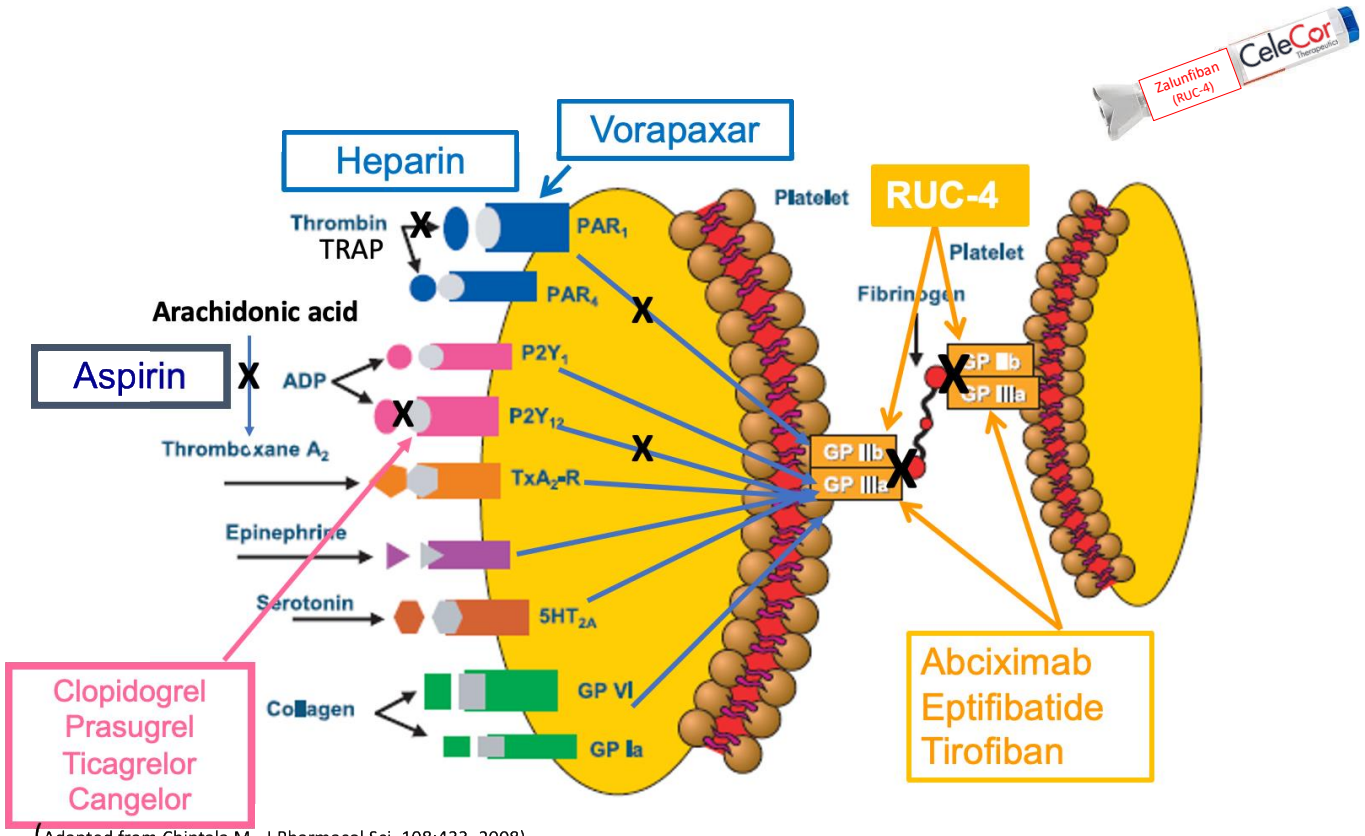
Celebrate Trial of Zalunfiban (GPIIbIIIa)

- Phase 3 Randomized placebo-controlled international multicenter study: study of two doses of zalunfiban v placebo
- Population: acute STEMI
- Intervention: Single s.c. injection by EMS of randomized study drug
- Treatment: all other treatment as per usual standard
- Study center: PAMC
- Consent: EFIC with brief EMS consent
- Principal Investigator: Jon McDonagh M.D.; Sub-PI: Michael Levy MD
- PAMC: Louise Cardenas and Andrea Castelblanco Pardo: Research Support Svc
- Primary endpoint: clinical outcome at 30 days

Zalunfiban is a next generation GPIIb/IIIa inhibitor that blocks platelet aggregation irrespective of which activation pathway is stimulated



(Adapted from Chintala M., J Pharmacol Sci. 108:433, 2008)

Comparison to Other Platelet Inhibitors

	Aspirin	Ticagrelor & Prasugrel	Tirofiban & Eptifibatide	Cangrelor	Selatogrel	**Zalunfiban**
Rapid onset			▯	▯	▯	♥
Easy to administer	▯	▯			▯	♥
Inhibits all platelet aggregation pathways			▯			♥
Can open a closed coronary artery[1]			▯			♥
Predictable response	▯		▯	▯		♥
Absorption independent of opioid administration			▯	▯		♥
Low risk of thrombocytopenia [1]	▯	▯		▯	▯	♥

CeleCor THERAPEUTICS

1 Being investigated in CeleCor's ongoing Phase 3 pivotal trial, CeleBrate.

Zalunfiban is the potential solution!!!

Zalunfiban Is a Next-generation GPIIb/IIIa Inhibitor

PROMPT

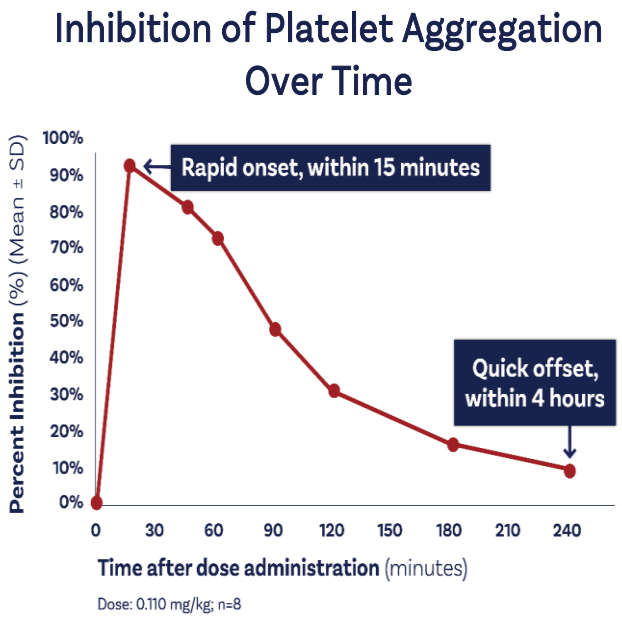
- Specifically designed for medical first responders and emergency personnel to administer by subcutaneous injection using an auto-injector

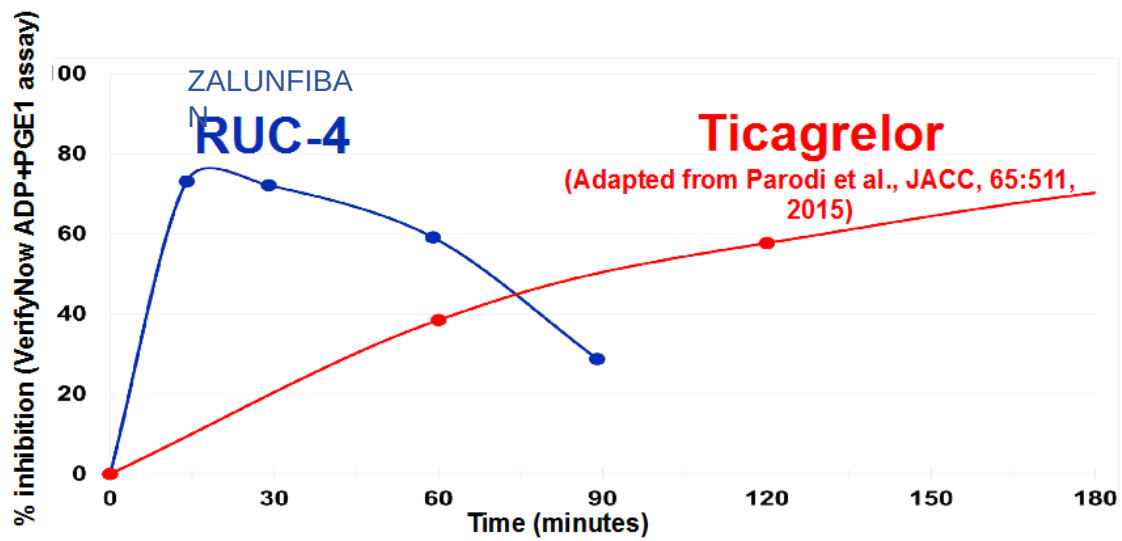
POTENT

- Reaches maximal effect within 15 minutes[1]

PREDICTABLE

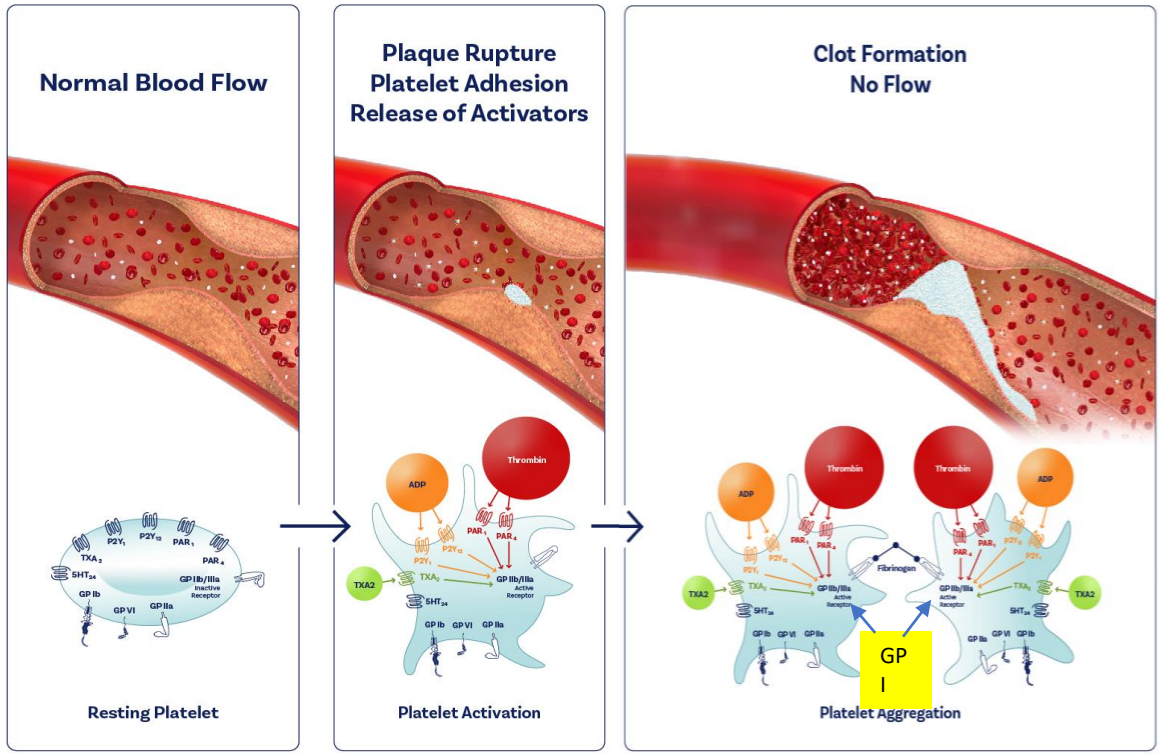
- Designed to offset quickly (<2 hours)
  - Increases safety and ease of later medical management





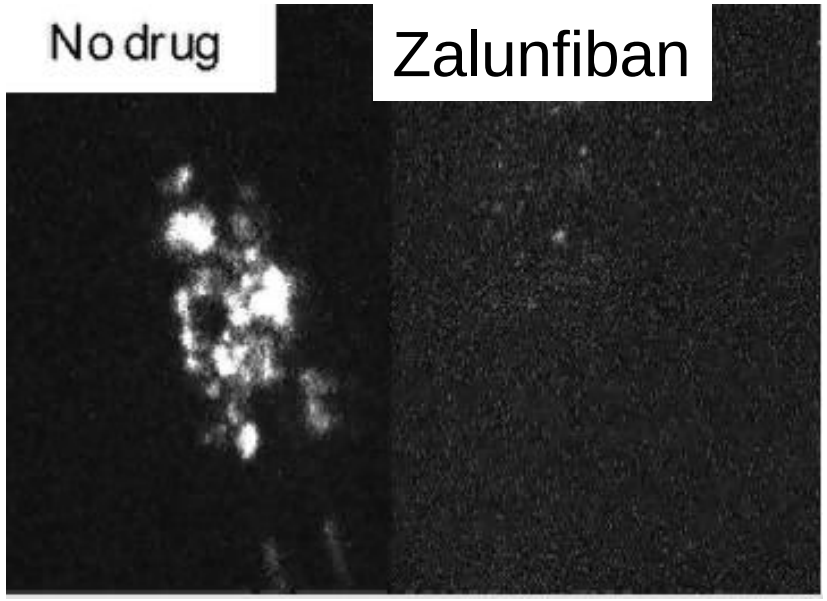
Adapted from Kereiakes et al., AHA Presentation, November 16, 2019

Platelets Critical in the First Hour



CeleCor THERAPEUTICS

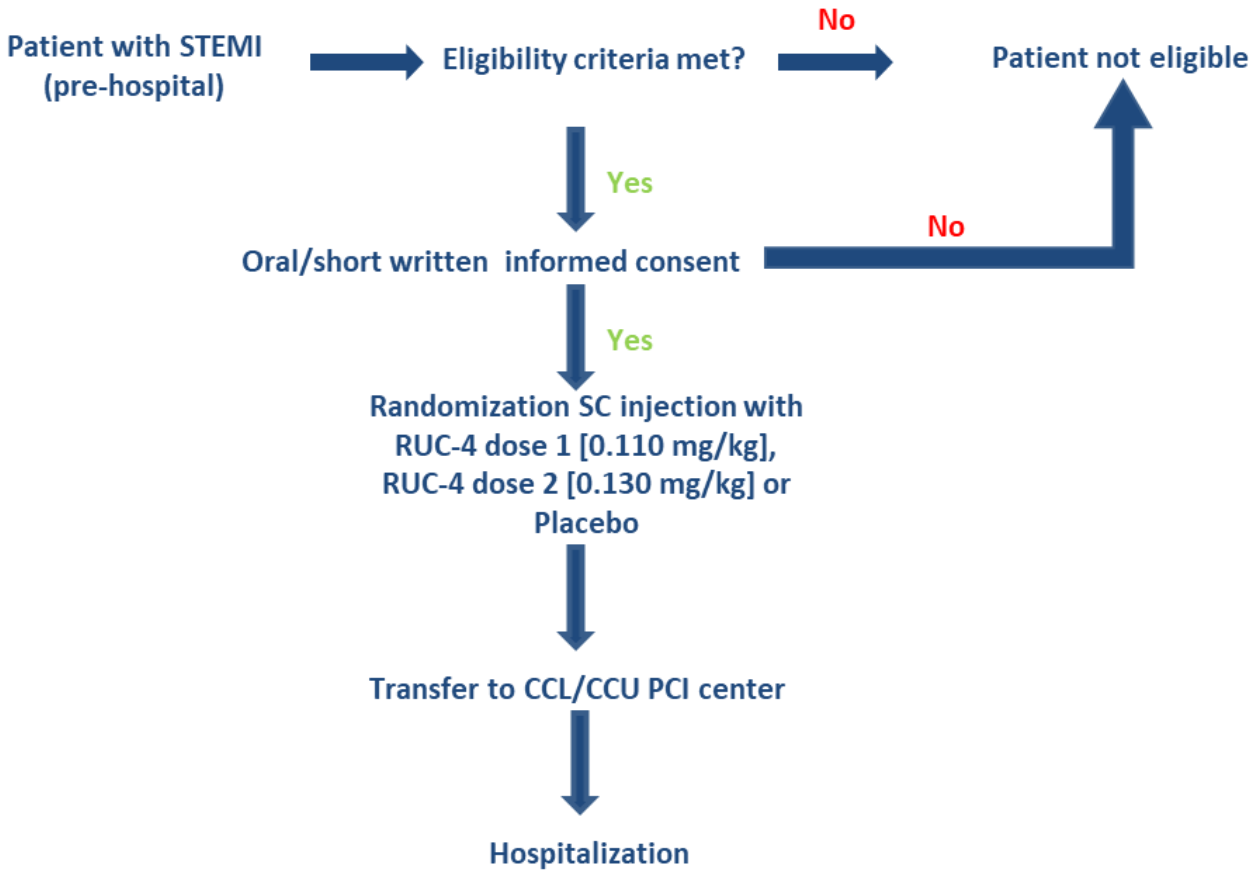
Zalunfiban Prevents Platelet Aggregation on Damaged Blood Vessels



Effect of RUC-4 (1.5 mg/kg IV) and Abciximab (0.25 mg/kg IV + Infusion) on Human Platelet Deposition After Laser Injury in Diacovo vWF Transgenic Mouse

(Li et al., ATVB 34:2321, 2014)

CEL-03: CELEBRATE Trial Design



https://clinicaltrials.gov/ct2/show/NCT04825743?term=celebrate&draw=2&rank=2

WILL PATIENT BE TAKEN TO A PARTICIPATING PCI HOSPITAL CLINICAL SITE ☐ **YES** ☐ **NO [STOP - do not enroll]**

Inclusion criteria:	**Yes**	**No**
- STEMI, presenting with new ST-elevation ≥ 2mm in ≥ 2 adjacent ECG leads, who would qualify for PCI	☐	☐
- Persistent ischemic chest pain for > 10 minutes and ≤ 4 hours (maximum)	☐	☐
- Male ≥ 18 years or post-menopausal or surgically sterile female ≥ 50 years	☐	☐
- Weight (estimated or by history) between 115-287 lbs	☐	☐
- Willing and able to give informed consent		

If **ALL** inclusion criteria are checked **'YES': review exclusion criteria:**

Exclusion criteria:	**Yes**	**No**
- CardioPulmonary Resuscitation (CPR) for **current** Out of Hospital Cardiac Arrest (OHCA)	☐	☐
- Cardiogenic shock (systolic blood pressure < 90 mmHg, confirmed on repeat testing and heart rate > 100 bpm)	☐	☐
- Current known active COVID-19 infection (according to local guidelines)	☐	☐
- Current treatment with dialysis (peritoneal and/or hemodialysis)	☐	☐
- Current treatment with oral anticoagulation [Vitamin-K antagonists: Coumadin, or DOAC: dabigatran, apixaban, edoxaban, rivaroxaban, betrixaban, or thrombolytic agents: tenecteplase, alteplase, reteplase, streptokinase, and urokinase:	☐	☐
- Major surgery, or trauma, or bleeding leading to hospitalization, within the past month	☐	☐
- Known history of ischemic or hemorrhagic stroke	☐	☐
- Known severe anemia (regular blood transfusion needed)	☐	☐
- Participation in another clinical study with investigational product or device within the past month	☐	☐
- Previously enrolled in this study	☐	☐
- Life expectancy less than one year	☐	☐

If **ALL** exclusion criteria are **'NO',** read OPT Out Script:

CeleBrate

EMS Overview

Step 1 Confirm STEMI (ECG)

Step 2 Check inclusion/exclusion criteria

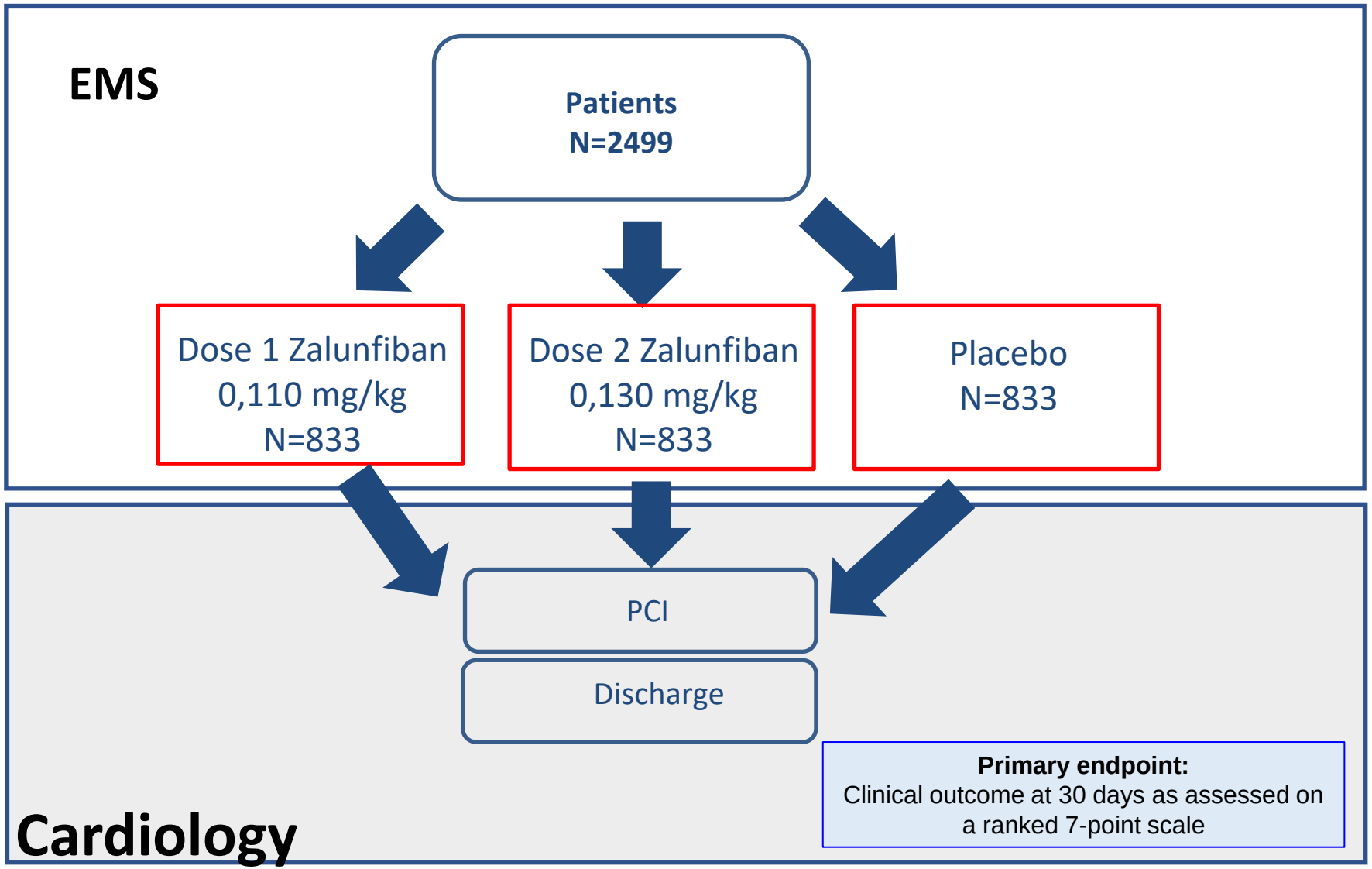
Step 3 Obtain verbal informed consent

CeleBrate

Step 4 Open study kit & check drug ok

Step 5 Draw up drug (weight based)

CeleBrate TRIAL



Status

- Enrolling in 5 Countries (Mexico, Canada, France, Netherlands, CZ Republic, Hungary, Romania, US)
- 1300 Patients enrolled. Excellent Safety Profile
- Trial approved by Advarra IRB
- Trial is approved by FDA under EFIC (using streamlined community engagement)
- All aspects of trial compensated by CeleCor

- US Sites: Alaska*, Austin, San Antonio, St. Louis, Detroit

Conclusion/Questions

- Trial has been ongoing in Europe: no safety issues after >1000 enrolled
- Promise of potential of recanalization in acute coronary thrombosis
- SC injection by EMS
- Fast onset
- Potent
- Short half life

- QUESTIONS?

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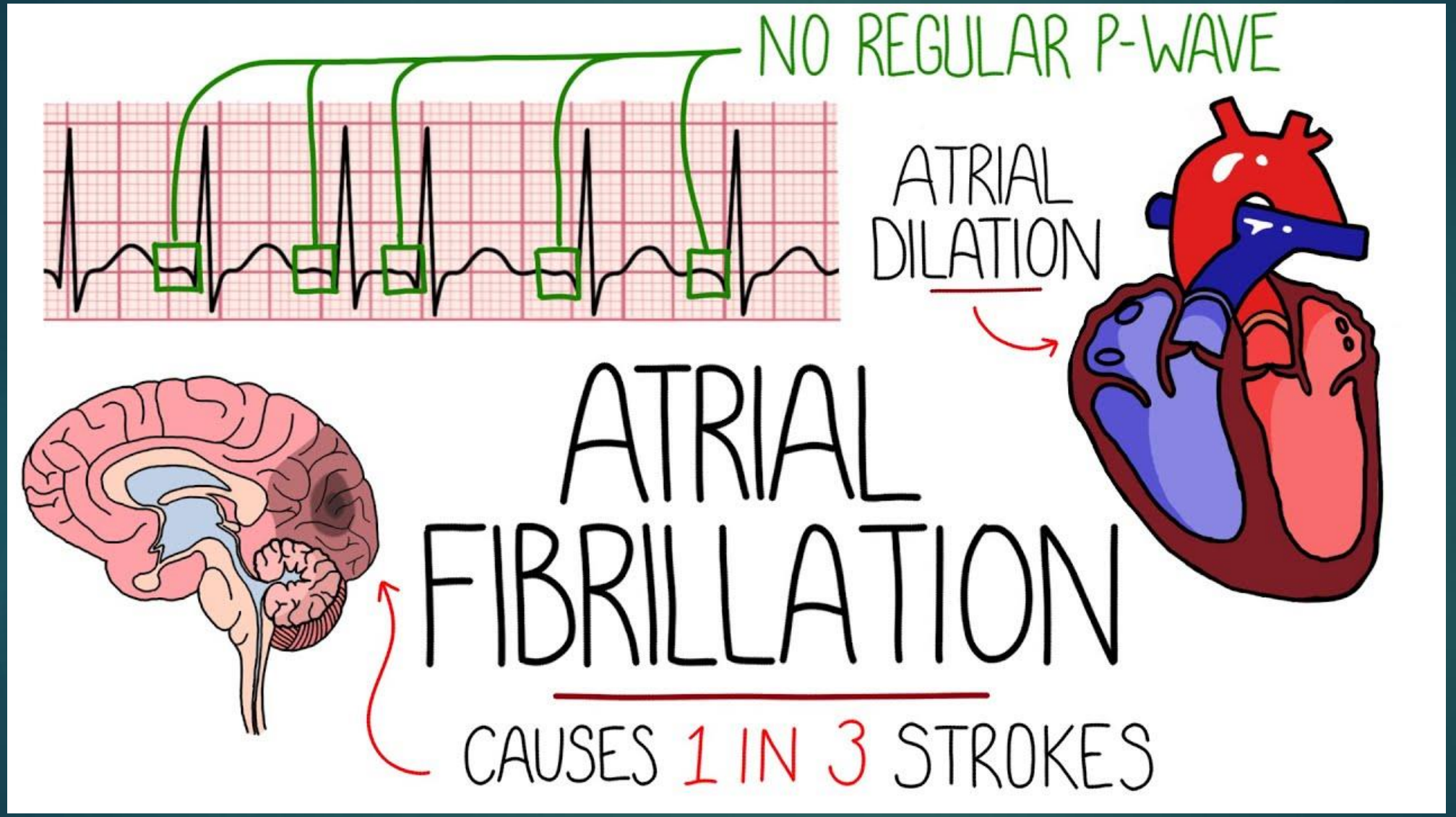
PLEASE JOIN THE EFFORT TO IIMPROVE TREATMENT OF PATIENTS WITH HEART ATTACKDS BEFORE THEY REACH THE HOSPITAL

What's the RX for the AF?

W. SCOTT GILMORE, MD, FACEP, FAEMS

Amateur [musicians] practice until they can get it right; professionals practice until they can't get it wrong

HAROLD CRAXTON


NO REGULAR P-WAVE
ATRIAL DILATION
ATRIAL FIBRILLATION
CAUSES 1 IN 3 STROKES

Atrial Fibrillation with Rapid Ventricular Response (RVR)

- Occurs when the ventricular response rate increases over 120 bpm
- Associated with
  - Decreased ventricular diastolic filling
  - Decreased cardiac output
  - Decreased coronary artery perfusion
- These physiologic changes can cause palpitations, shortness of breath, and chest pain

Two Main Treatments of Atrial Fibrillation with Rapid Ventricular Response

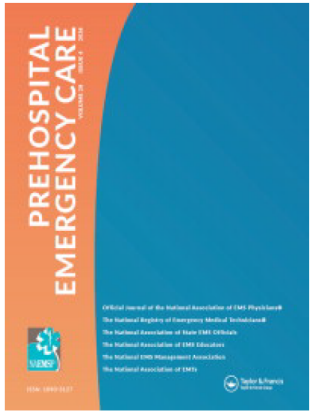
- Rhythm control
  - Reserved for hemodynamically unstable patients
  - Synchronized cardioversion in the prehospital setting
- Rate control
  - Stable, symptomatic patients
  - Calcium channel blockers
    - Decrease ventricular response by slowing conduction and prolonging the refractory period in the atrioventricular (AV) node
    - Most commonly used CCB in the prehospital setting is diltiazem

Should Patients with AF-RVR be Treated in the Prehospital Setting or Have Treatment Delayed Until Arrival at the Emergency Department?

Historical Studies

- Some descriptive case studies have demonstrated that prehospital a fib with RVR is safe and effective
  - Rostango et all (1991)
  - Rodriquez et al (2019)
  - Luk et al (2013)
- Another concluded prehospital interventions may be unnecessary
  - Abarbanell et al (2003)

- Only comparative analysis showed that those who are administered diltiazem achieved prehospital rate or rhythm control more frequently (81% vs 17%)
  - Wang et al (2001)



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Prehospital Emergency Care

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Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

Louis B. Fornage, Christine O'Neil, Stephen R. Dowker, Eric R. Wanta, Ryan S. Lewis & Lawrence H. Brown

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Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

- This study explored whether prehospital ALS rate or rhythm control interventions improve prehospital and hospital outcomes for patients presenting to EMS with AF- RVR.
- The *a priori* primary outcome measure was discharge to home from the ED.
- Additional outcomes included achieving rate control prior to ED arrival, ED and hospital length of stay for discharged and admitted patients respectively, and mortality.
- The frequency of adverse events was also evaluated.

Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

- Inclusion Criteria
  - 9-1-1 scene responses
  - Atrial fibrillation documented as the first electrocardiogram interpretation
  - Initial pulse rate of 110 bpm or higher

- Exclusion Criteria
  - Patients less than 16 years of age or greater than 100 years of age
  - Trauma patients with a concurrent medical complaint
  - Patients with documented fever (temperature ≥ 100.4° F) or hypothermia (temperature <96.8° F) potentially indicating sepsis
  - Patients who experienced cardiac arrest prior to arrival

Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

Table 4. Propensity score matched outcomes for AF-RVR patients with and without prehospital intervention.

	Untreated Patients		Treated Patients			
Outcome	N Analyzed	Outcome	N Analyzed	Outcome	Propensity Score Matched ATET (CI)	NNT (CI)
Prehospital Rate Control Achieved,[a] n (%)	4,859	885 (18.2)	4,859	1,994 (41.0)	+22.8 (+21.1; +24.6)	5 (4–5)
Discharged to Home, n (%)	1,347	458 (34.0)	1,347	510 (37.9)	+3.9 (+0.2; +7.5)	26 (14–500)
ED Length of Stay, Median (IQR) hours[b]	495	5.5 (3.7–22.7)	445	5.1 (3.3–21.6)	−0.4 (-1.6; +0.8)	n/a
Hospital Length of Stay, Median (IQR) days[c]	745	4.6 (2.9–7.6)	774	4.2 (2.7–7.2)	−0.4 (-0.8; +0.03)	n/a
Mortality, n (%)	1,343	90 (6.7)	1,346	58 (4.3)	−2.5 (-4.2; −0.8)	40 (24–125)

Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

Table 5. Adverse events in propensity score matched AF-RVR patients who did and did not receive prehospital intervention.

	Matched Patients		
	Untreated	Treated	ATET (CI)
N	4,859	4,859	
Bradycardia, n (%)	178 (3.7)	177 (3.6)	−0.02 (-0.8; +0.7)
Non-transient Bradycardia, n (%)	45 (0.9)	42 (0.9)	−0.1 (-0.4; +0.3)
Bradycardia before Intervention, n	n/a	47	n/a
Intervention to Onset, median (IQR) min[a]	n/a	11 (6–17)	n/a
Hypotension, n (%)	351 (7.2)	477 (9.8)	+2.6 (+1.5; +3.7)
Non-transient Hypotension, n (%)	144 (3.0)	126 (2.6)	−0.4 (-1.0; +0.3)
Hypotension before Intervention, n	n/a	129	n/a
Intervention to Onset, median (IQR) min[a]	n/a	7 (3–12)	n/a
Cardiac Arrest, n (%)	5 (0.1)	10 (0.2)	+0.1 (-0.1; +0.3)
Cardiac Arrest at ED Arrival, n (%)	0 (0.0)	2 (<0.1)	+0.02 (-0.01; +0.1)
Cardiac Arrest before Intervention, n	n/a	7	n/a
Intervention to Onset, median (IQR) min[a]	n/a	3 (2–3)	n/a

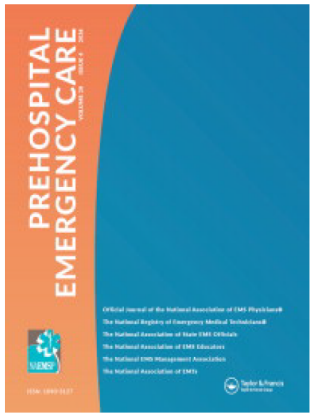
Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

	Prehospital Outcomes Cohort	Hospital Outcomes Cohort	Initial Dosing, mg	
			Median (IQR)	Minimum; Maximum
N	4,859	1,347		
Any medication, n (%)	4,761 (98.0)	1,321 (98.1)	n/a	n/a
diltiazem, n (%)	4,082 (84.0)	1,141 (84.7)	15 (10-20)	5; 30
beta-blocker, n (%)	263 (5.4)	92 (6.8)	5 (5-5)	2.5; 15
adenosine, n (%)	234 (4.8)	49 (3.6)	6 (6-6)	6; 12
amiodarone, n (%)	133 (2.7)	28 (2.1)	150 (150-150)	150; 300
verapamil, n (%)	22 (0.5)	0 (0.0)	5 (5-5)	2.5; 10
other medication, n (%)	27 (0.6)	11 (0.8)	n/a	n/a
Cardioversion	98 (2.0)	26 (1.9)	n/a	n/a

Prehospital Intervention Improves Outcomes for Patients Presenting in Atrial Fibrillation with Rapid Ventricular Response

- In this propensity score matched study of patients receiving prehospital treatment were mor likely to achieve rate control prior to arrival at the ED (NNT = 5), more likely to be discharged home from the ED (NNT = 26), and less likely to die (NNT = 40).

Is Diltiazem Safe in the Prehospital Setting?



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Prehospital Emergency Care

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Efficacy and Safety of Prehospital Diltiazem

Ellen Pil, Matthew Levy, Timothy Chizmar, Ruben Troncoso, Eric Garfinkel & Asa Margolis

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Efficacy and Safety of Prehospital Diltiazem

- Retrospective observational study of the Maryland Institute for Emergency Medical Services Systems (MIEMSS) database
- Primary outcome variable for this study was the proportion of patients who clinically improved at the time of hospital arrival
- Secondary outcome was the proportion of patients who achieved rate control (HR <100 bpm)at the time of hospital arrival
- Additional outcome was the proportion of patients who experienced hypotension (<90 mmHg) or bradycardia (<60 beats per minute) that require a rescue intervention (transcutaneous pacing or the administration of calcium chloride, atropine, dopamine, or epinephrine) or persisted at the time of hospital arrival

Efficacy and Safety of Prehospital Diltiazem

- Adult patients with symptomatic atrial fibrillation or flutter with a HR ≥ 100 beats per minute and a SBP ≥ 100 mmHg

- Initial IV diltiazem bolus over 2 minutes of 0.25 mg/kg (maximum 20 mg)
- Second dose of 0.35 mg/kg (maximum 25 mg) if the initial response is inadequate after 15 minutes

- Initial bolus of 5-10 mg for patients who are older than 50 years of age, or have borderline hypotension, renal failure or congestive heart failure

Efficacy and Safety of Prehospital Diltiazem

Table 1. Median values of studied characteristics among patients receiving diltiazem for rapid atrial fibrillation/atrial flutter.

Measure	Median [IQR]
Age (years)	72 [61, 80]
Encounter Length (minutes)	34 [28, 41]
Maximum Heart Rate (bpm)	168 [152, 183.75]
Final Heart Rate (bpm)	120 [96, 144]
Final Heart Rate / Maximum Heart Rate	0.73 [0.58, 0.87]
Maximum Systolic Blood Pressure (mmHg)	153 [138, 171]
Final Systolic Blood Pressure (mmHg)	132 [117, 150]
Total Diltiazem Dose (mg)	10 [10, 20]
Intravenous Fluid Volume (mL)	0 [0, 250]

Efficacy and Safety of Prehospital Diltiazem

Table 2. Frequency of safety and efficacy outcomes among patients receiving diltiazem for rapid atrial fibrillation/atrial flutter.

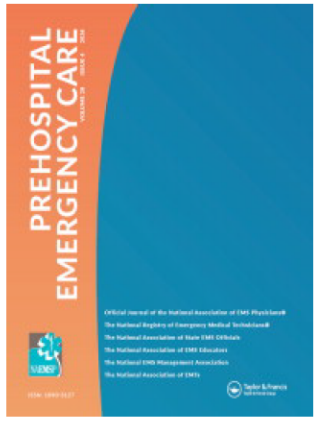
Measure	Frequency (%)
Rate Control[a]	604/2216 (27.3%)
Clinical Improvement[b]	1414/2216 (63.8%)
Any Adverse Event	78/2254 (3.5%)
Both hypotension and bradycardia	8/2254 (0.4%)
Hypotension only	40/2254 (1.8%)
Bradycardia only	30/2254 (1.3%)

[a]Defined as final heart rate 60–100 bpm.
[b]Defined as a final heart rate of 60–100 bpm or >20% decrease from the maximum heart rate.

Efficacy and Safety of Prehospital Diltiazem

- Diltiazem is safe and effective when given to treat rapid atrial fibrillation in the prehospital setting with specific caveats
- The incidence of adverse events increase with baseline SBP <140 mmHg, HR <120 BPM, and concurrent nitroglycerin administration
- Patients over the age of 50 are less likely to have clinical improvement from diltiazem administration

Is There a Specific Way Diltiazem Should be Administered?



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Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?

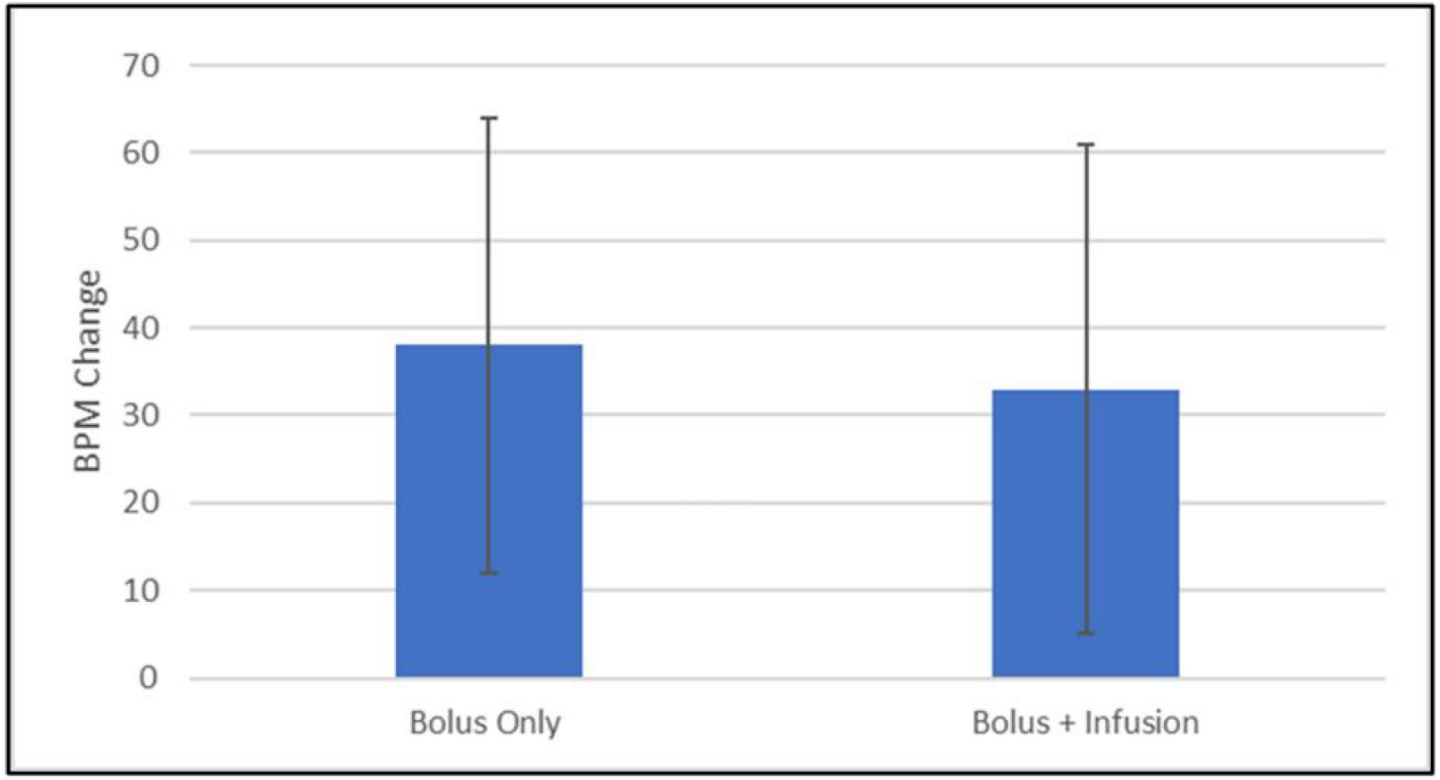
Michael Berkenbush, Nicholas Sherman, Nikhil Jain & Peter Cosmi

To cite this article: Michael Berkenbush, Nicholas Sherman, Nikhil Jain & Peter Cosmi (21 May 2024): Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?, Prehospital Emergency Care, DOI: 10.1080/10903127.2024.2349745

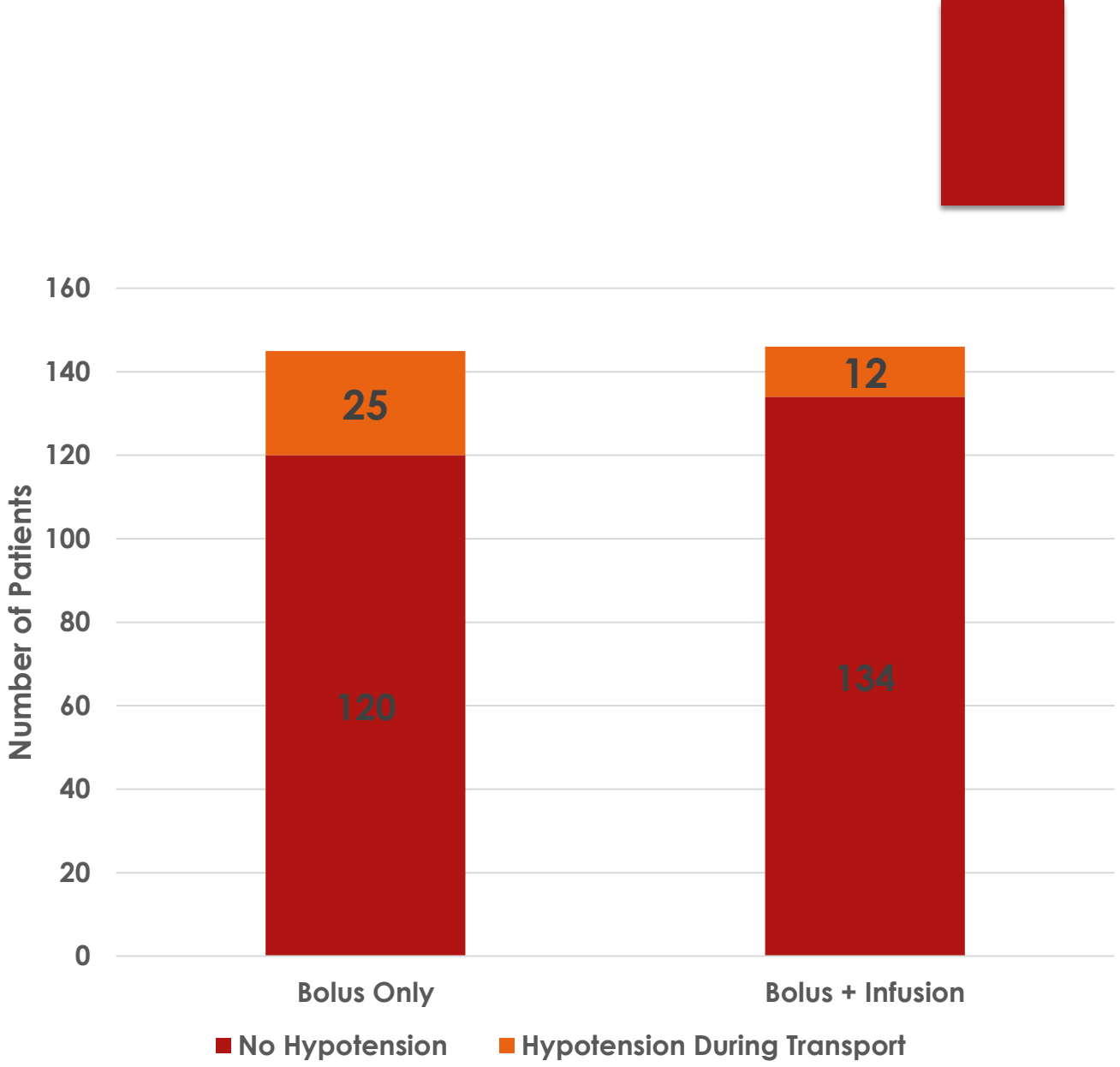
Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?

	BO	BI	Significance
Age (mean)	75.3	75.5	p = 0.89
Male (n,%)	71, 48.9%	65, 44.5%	p = 0.45
AF history (n, %)	103, 71.0%	105, 71.9%	p = 0.87
Initial HR (mean)	149.2	150.6	p = 0.59
Initial systolic BP (mean)	132.9	137.2	p = 0.19
Initial diastolic BP	85.1	87.8	p = 0.21
Initial diltiazem bolus (mg)	14.2	17.4	p <0.001

Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?



Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?



Prehospital Treatment of Atrial Fibrillation: Infusion Pump for Bolus and Infusion?

- Our results show no significant difference in HR control or need for repeat bolus at the ED with the use of diltiazem infusion following a diltiazem bolus compared to a bolus alone.

- However, even when administering a larger bolus, the use of an infusion pump resulted in less hypotension, likely related ti greater control of the rate of administration.

Diltiazem Precautions

- May precipitate shock by undermining compensation mechanism
  - Especially if the patient's tachycardia is compensatory for underlying pathology
    - Sepsis
    - Trauma
- Risk versus benefit should always be considered prior to administration

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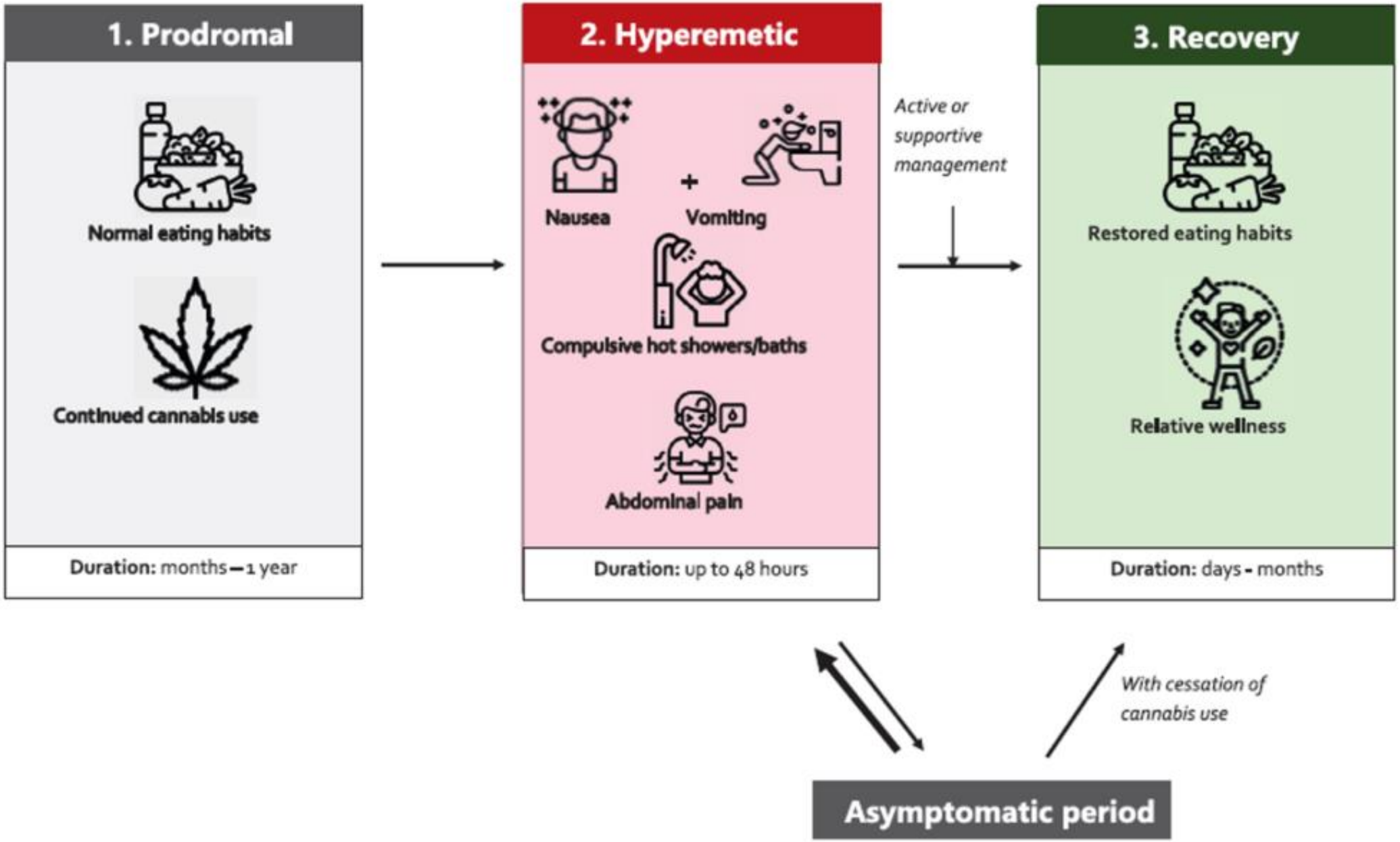
Questions

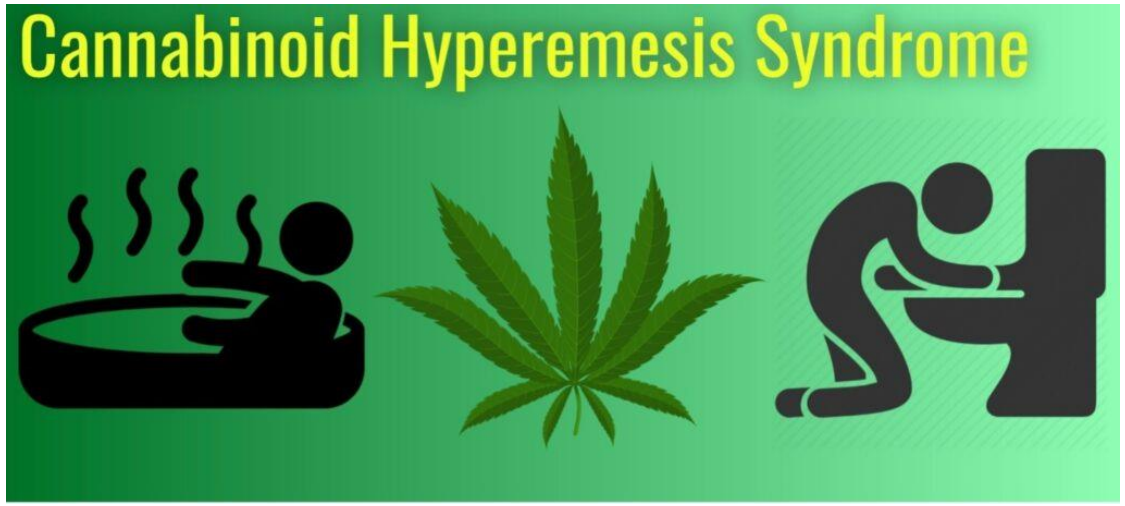
Rebuking the Puking?

Cannabinoid Hyperemesis Syndrome

W. Scott Gilmore, MD, FACEP, FAEMS

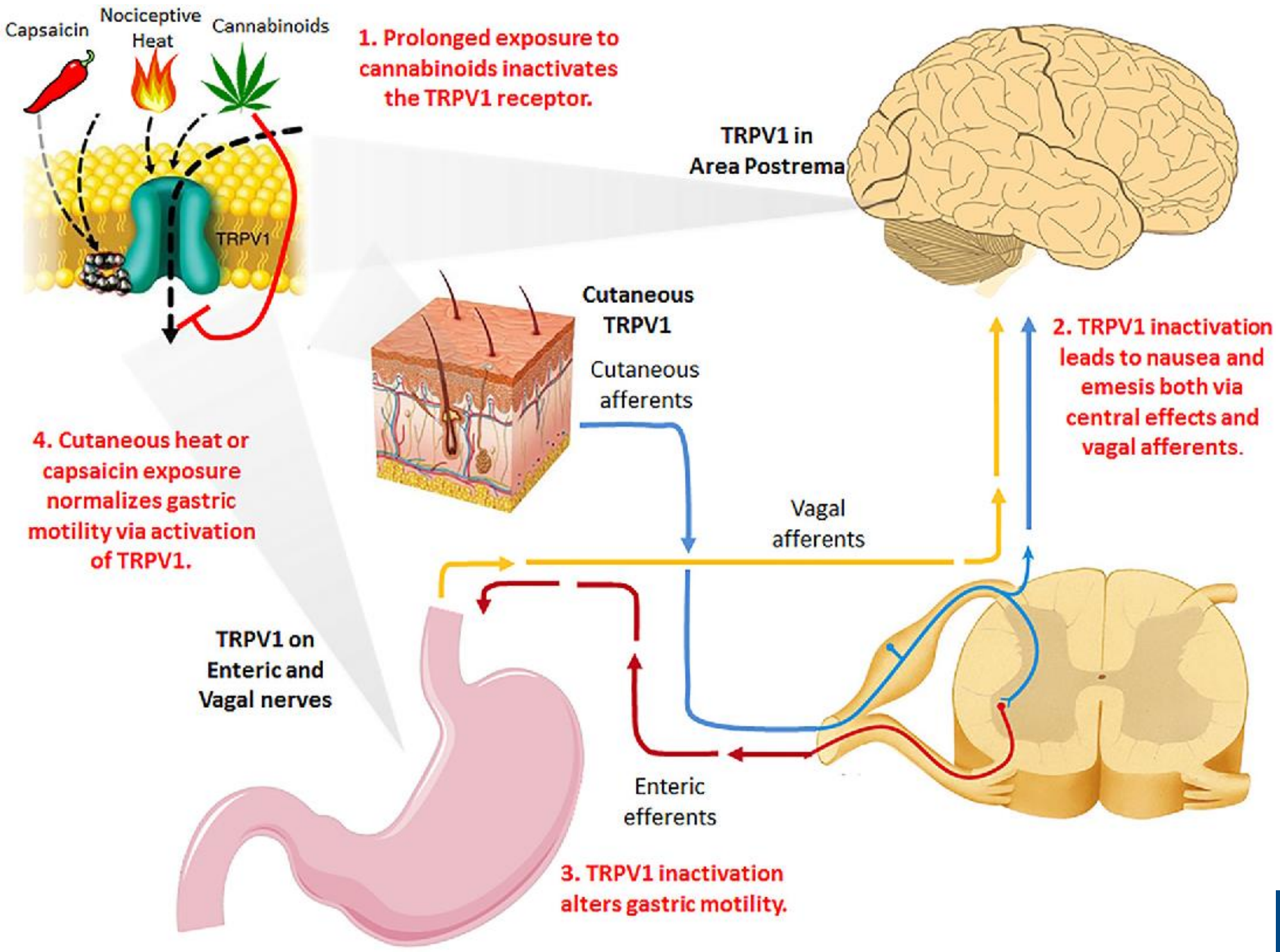

1. Prodromal
Normal eating habits
Continued cannabis use
Duration: months—1 year
2. Hyperemetic
Nausea
+
Vomiting
Compulsive hot showers/baths
Abdominal pain
Duration: up to 48 hours
Active or supportive management
3. Recovery
Restored eating habits
Relative wellness
Duration: days - months
With cessation of cannabis use
Asymptomatic period

Symptoms of Cannabinoid Hyperemesis Syndrome



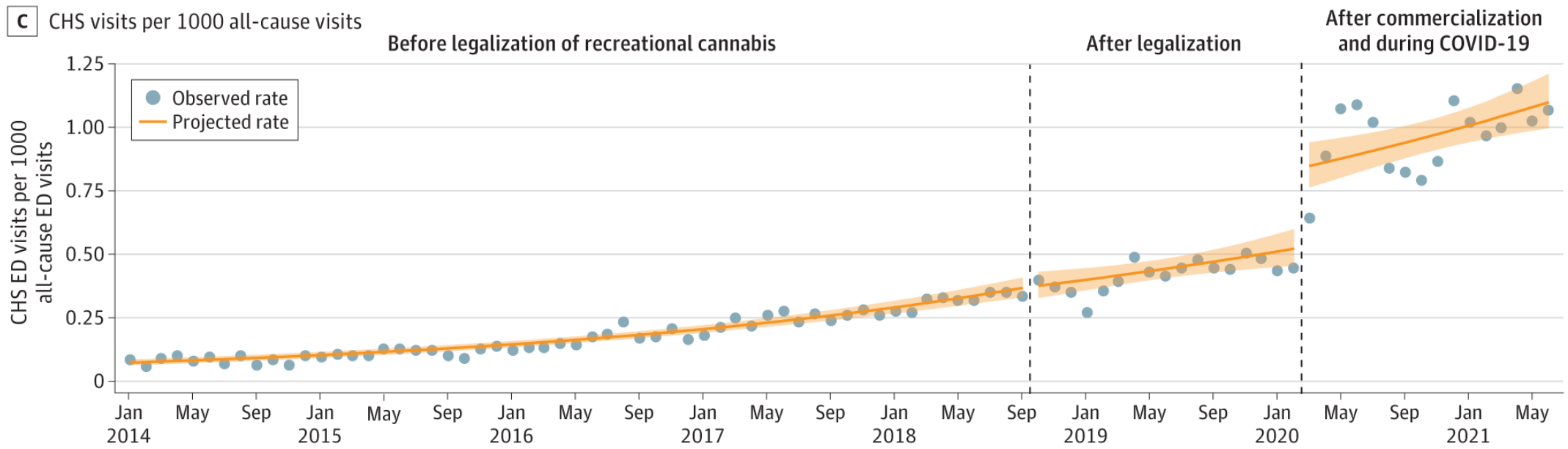
- Severe cyclic nausea and vomiting
- Epigastric or umbilical pain
- Symptoms present on waking up
- Symptoms improve when cannabis stopped
- Minimum of weekly cannabis use
- Weight loss
- Symptoms relieved by hot baths and showers
- Normal bowel habits

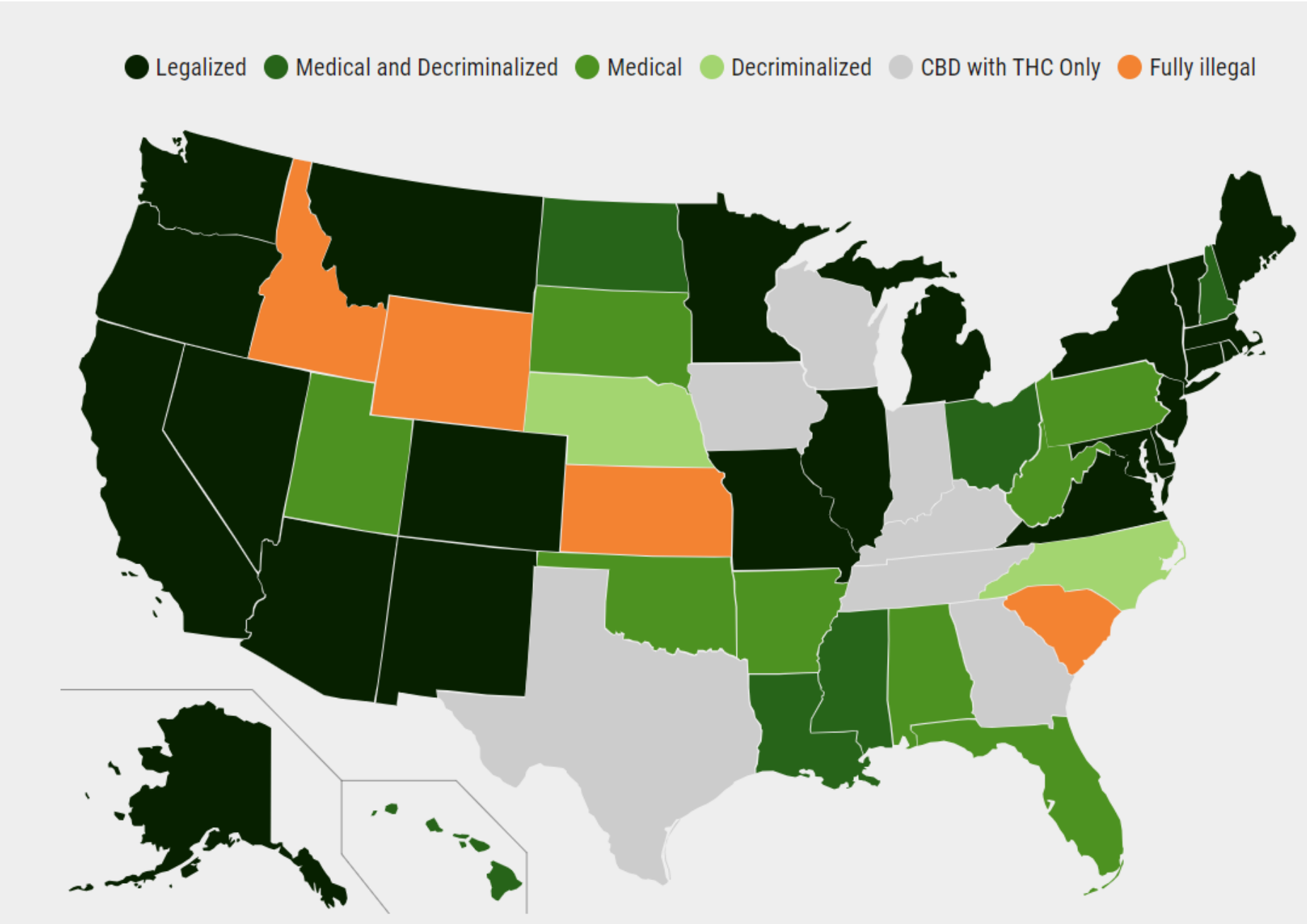
Why This Happens



How Common is CHS

- The incidence of CVS/CHS has nearly doubled since legalization of cannabis in Colorado.
- In one convenience sample of a busy urban emergency department, 32.9% (51/155) of patients who smoke marijuana 20 or more days per month reported symptoms of CHS
- In a retrospective review of an integrated health system, 16.51% (53/321) were suspected of having CHS




Legalized
Medical and Decriminalized
Medical
Decriminalized
CBD with THC Only
Fully illegal

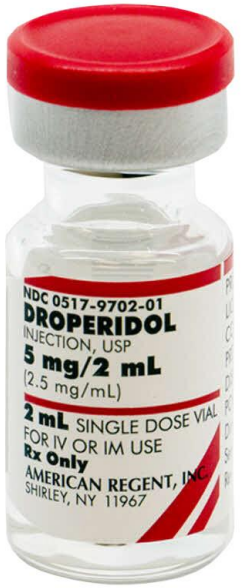
Definitive Treatment

The only effective way to permanently alleviate symptoms of Cannabinoid Hyperemesis Syndrome is stopping cannabis use.

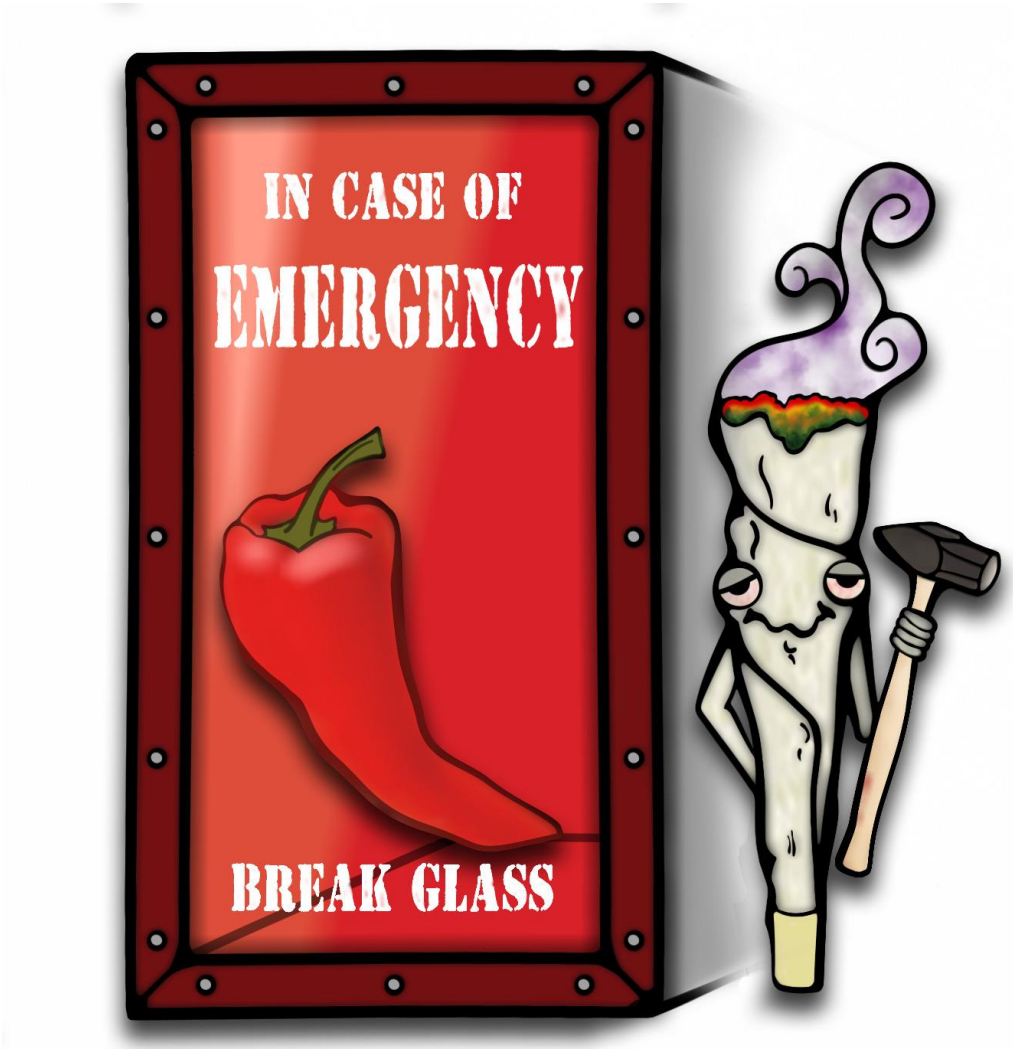
Why Treat Acutely

Acute management of symptoms is important for preventing dehydration and adrenal injury, common complications of CHS that can be fatal

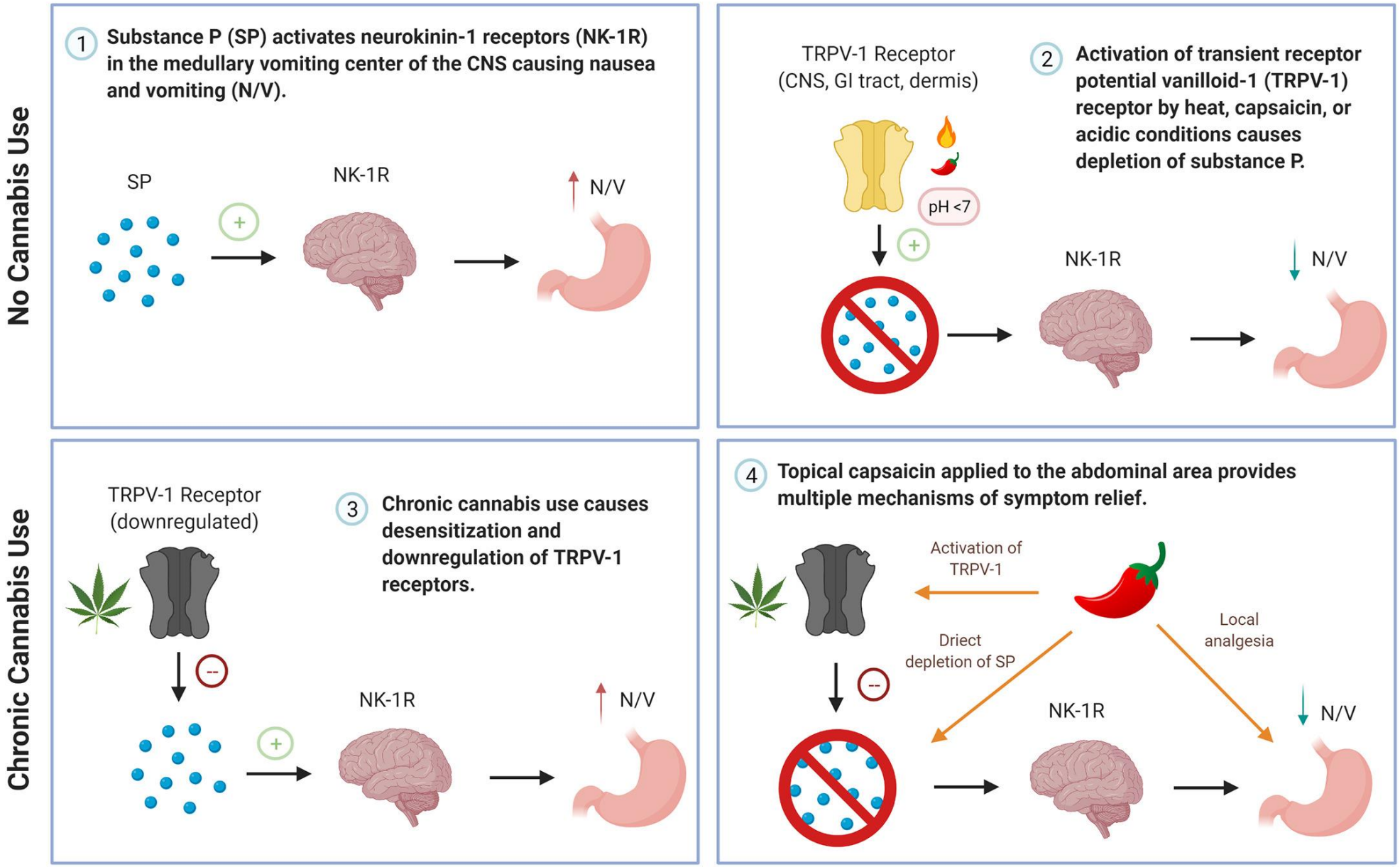
Anti-dopaminergic Anti-psychotics



Capsaicin Cream

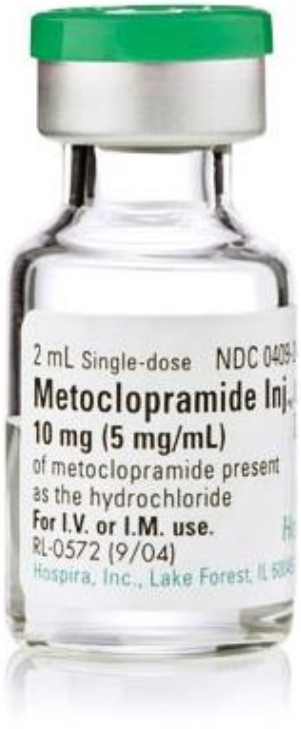


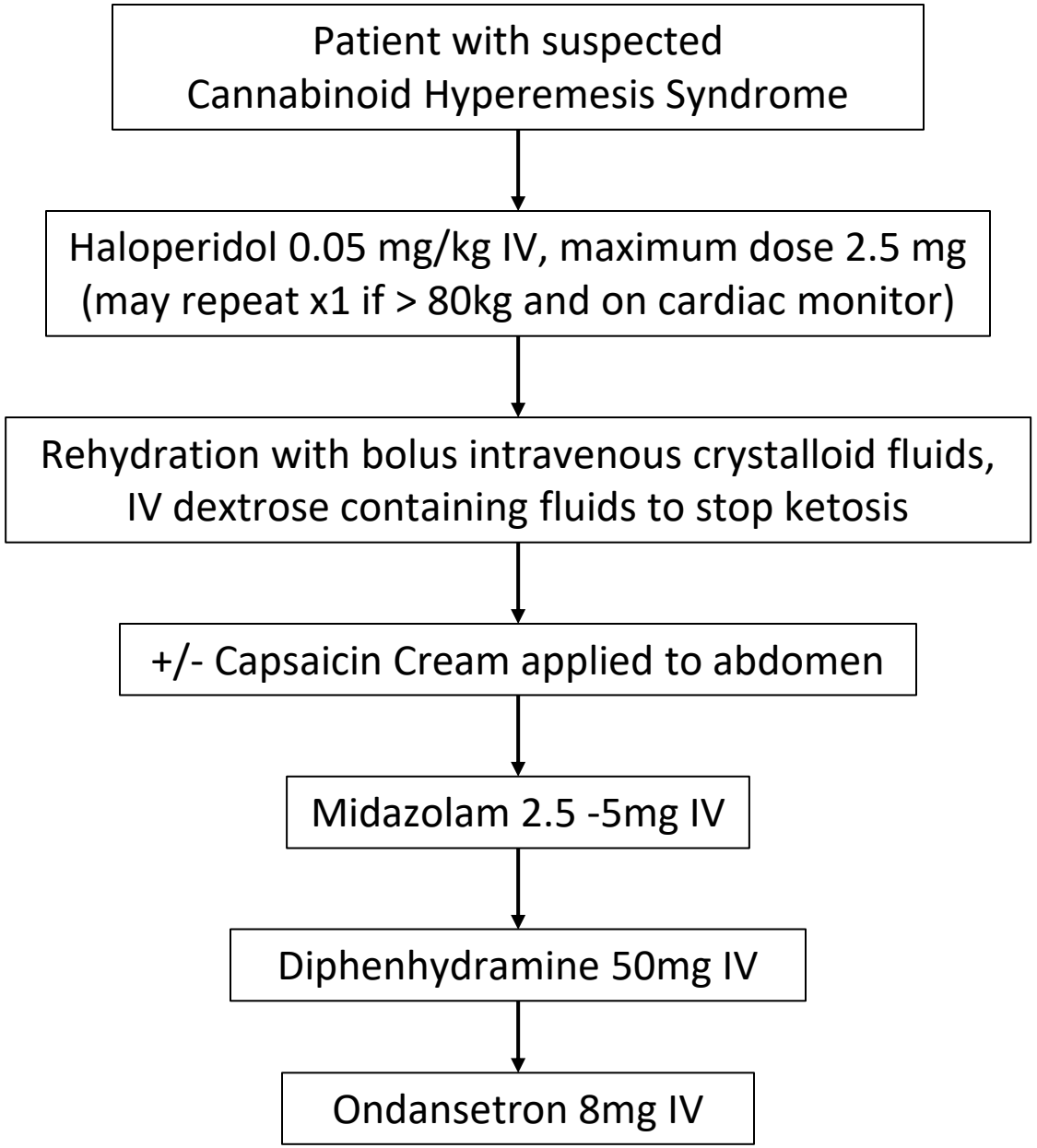
Mechanism of Capsaicin for Cannabinoid Hyperemesis Syndrome



Maybe She's Right

Ineffective Treatments




Patient with suspected
Cannabinoid Hyperemesis Syndrome
Haloperidol 0.05 mg/kg IV, maximum dose 2.5 mg
(may repeat x1 if > 80kg and on cardiac monitor)
Rehydration with bolus intravenous crystalloid fluids,
IV dextrose containing fluids to stop ketosis
+/- Capsaicin Cream applied to abdomen
Midazolam 2.5 -5mg IV
Diphenhydramine 50mg IV
Ondansetron 8mg IV

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Questions

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