UTAH SOCIETY OF HEALTH-SYSTEM PHARMACISTS

Annual Meeting
September 12, 2020

The Pharmacist's Role in Pandemic Planning in the Emergency Department

What to Do When You Don't Know What to Do!

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Disclosure

Instructions:

The speaker has no conflicts of interest to disclose.

The speaker will not be discussing any off-label uses of drugs.

Learning Objectives

At the conclusion of this activity, ***pharmacists*** should be able to successfully:

1. Articulate the various roles of pharmacists in an interdisciplinary team creating pandemic plans in the emergency department.

Learning Objectives

At the conclusion of this activity, ***pharmacy technicians*** should be able to successfully:

1. Explain why frequent changes in product selection, policy, and procedures during a pandemic or disaster management response occur.

What is Disaster Response?

- WHO defines a disaster as a sudden phenomenon of sufficient magnitude to overwhelm the resources of a hospital, region, or location requiring external support
- A thoughtful fast approach in response to a disaster is critical.
- The emergency medicine approach is quite similar to Dr. Michael Ryan, Executive Director, WHO Health Emergencies Program

How can we mitigate this situation to be less bad than it could possibly be?

Are we prepared for something bad if it happens?

Do we have the resources to respond?

How will we recover from this?

We all have emergency preparedness skills

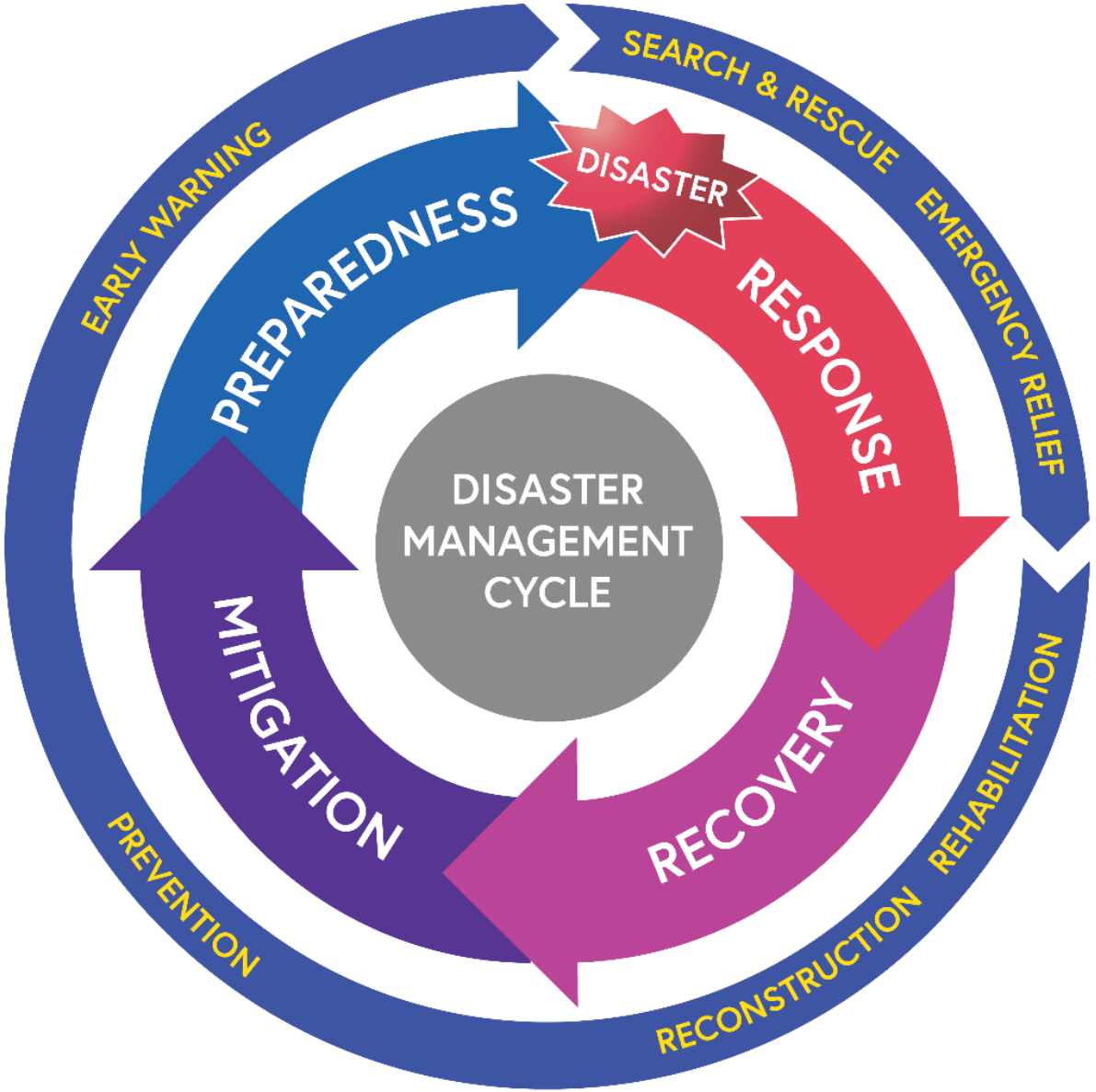
https://now.uiowa.edu/2014/03/safety-first-children

We all have emergency preparedness skills

https://now.uiowa.edu/2014/03/safety-first-children

We all have emergency preparedness skills

https://store.medicinesafe.com/products/medication-carrying-case
https://local12.com/news/local/1st-federal-opioid-crisis-trial-to-focus-on-distribution



Preparedness Cycle

- Preparedness
- Prevention
- Response
- Recovery
- Mitigation

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How can we mitigate this situation to be less bad than it could possibly be?

Are we prepared for something bad if it happens?

Do we have the resources to respond?

How will we recover from this?

Disaster Role(s) of a Pharmacist in the ED

ASHP Guideline on Emergency Medicine Services

- "It is essential that Emergency Medicine Pharmacists (EMP), in conjunction with the department of pharmacy, participate in emergency preparedness planning."
- "Planning and involvement should occur at a minimum at the institutional level….knowledge of local, state, and national emergency preparedness plans, programs, and support systems is paramount."

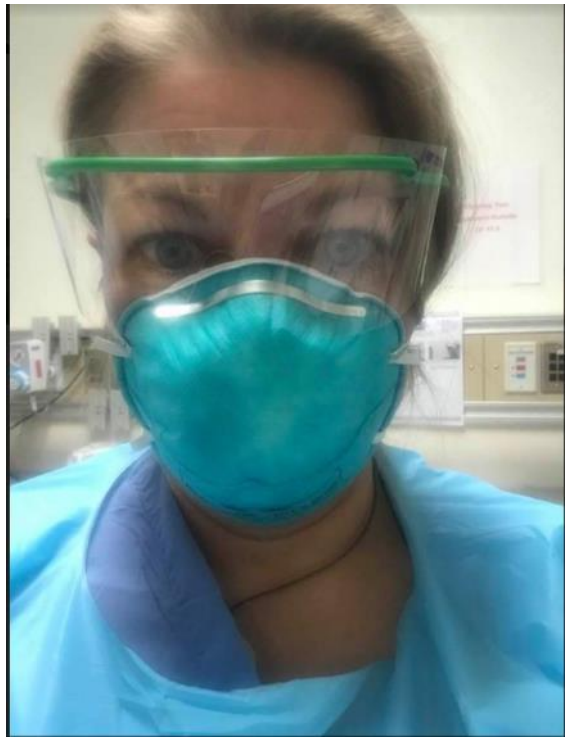
- American Society of Health-System Pharmacists. ASHP statement on the role of health-system pharmacists in emergency preparedness. Am J Health-Syst Pharm. 2003; 60:1993–5.

Disaster Role(s) of a Pharmacist in the ED

- Draw on your experience of the past to do better in the future
  - Katrina
  - H1N1
  - Ebola
  - TRAINING!

- American Society of Health-System Pharmacists. ASHP statement on the role of health-system pharmacists in emergency preparedness. Am J Health-Syst Pharm. 2003; 60:1993–5.

Did I mention training?



Support Documents for Pharmacy Involvement

ASHP Statement on the Role of Health-System Pharmacists in Emergency Preparedness

Emergency and Disaster Preparedness and Response Planning: A Guide for Boards of Pharmacy

A Pharmacist's Guide to Pandemic Preparedness
- APhA, ASHP, NACDS in 2007

Pharmacist as Front-Line Responders for COVID-19 Patient Care
- Joint Executive Summary by all major Rx orgs

ASHP Guidelines on Emergency Medicine Pharmacist (EMP) Services

Pharmacy Leader's Role in Hospital Emergency Preparedness Planning

- American Society of Health-System Pharmacists. ASHP statement on the role of health-system pharmacists in emergency preparedness. Am J Health-Syst Pharm. 2003; 60:1993–5.
- https://nabp.pharmacy/wp-content/uploads/2016/07/08Emergency_Preparedness_Guide.pdf
- https://www.pharmacist.com/sites/default/files/files/APHA%20Meeting%20Update/PHARMACISTS_COVID19-Final-3-20-20.pdf
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- American Society of Health-System Pharmacists. ASHP guidelines on emergency medicine pharmacist services. Am J Health-Syst Pharm. 2011; 68:e81–95.
- Bell C. *Hospital Pharmacy*. Pharmacy Leader's Role in Hospital Emergency Preparedness Panning. 2014 (Apr); 49(4): 398-404.

Other Training for Pharmacist and Technician Involvement

Emergency Preparedness

- AHLS
- Basic Disaster Life Support
- Advanced Disaster Life Support
- National Incident Management System
  - Free online training @ www.FEMA.gov
- Disaster Medical Assistance Teams
  - Emergency Medication Assistance Program

Assess the Scene:

Jan 22, 2019: Received first communication from our ED Code Bio Coordinator

- *Mask the patient, limit contact, place in airborne precautions…*

Interim 2019 novel coronavirus (2019-nCoV) patient under investigation (PUI) form

As soon as possible, notify and send completed form to: 1) your local/state health department, and 2) CDC: email (eocreport@cdc.gov, subject line: nCoV PUI Form) or fax (770-488-7107). If you have questions, contact the CDC Emergency Operations Center (EOC) at 770-488-7100.

Today's date_____ **State patient ID**_____ **NNDSS local record ID/Case ID**[1] _____ **State**___ **County**_____

Interviewer's name_____ **Phone**_____ **Email**_____

Physician's name _____ **Phone**_____ **Pager or Email**_____

Sex ☐ M ☐ F **Age**_____☐ yr ☐ mo **Residency** ☐ US resident ☐ Non-US resident, country_____

PUI Criteria

Date of symptom onset_____

Does the patient have the following signs and symptoms (check all that apply)?

☐ Fever[2] ☐ Cough ☐ Sore throat ☐ Shortness of breath

In the 14 days before symptom onset, did the patient:

Spend time in Wuhan City, China? Does the patient live in Wuhan City? ☐ Y ☐ N ☐ Unknown Date traveled **to** Wuhan City_____ Date traveled **from** Wuhan City_____ Date **arrived** in US_____	☐ Y ☐ N ☐ Unknown
Have close contact[3] with a person who is under investigation for 2019-nCoV while that person was ill?	☐ Y ☐ N ☐ Unknown
Have close contact[3] with a laboratory-confirmed 2019-nCoV case while that case was ill?	☐ Y ☐ N ☐ Unknown

Assess the Scene:

January 23, 2020: Chinese government locks down Wuhan

https://abcnews.go.com/Health/timeline-coronavirus-started/story?id=69435165

Assess the Scene:

January 30, 2020
- WHO declares a “global health emergency”

February 4, 2020
- The “Diamond Princess” is quarantined off the coast of Yokohama, Japan

https://www.forbes.com/sites/victoriaforster/2020/03/22/what-have-scientists-learned-from-using-cruise-ship-data-to-learn-about-covid-19/#290c9787406d

Assess the Scene:

March 3, 2020
- First official communication from management

March 6, 2020
- First patient in Utah

SALT LAKE CITY (KUTV) — Utah health officials have confirmed the first known case of COVID-19, known as the coronavirus, in Utah.

Jim Spiewak reports (KUTV)

https://kutv.com/news/local/first-coronavirus-case-confirmed-in-utah

Disaster Role(s) of an EMP: Patient Care

ED: Still open for business

- "Normal" patient care
  - Resuscitation
  - Medication management, safety, and optimization
  - Response to critical events or procedures
    - Rapid Sequence Intubation
    - ACLS

COVID-19

- COVID-19 complicated clinical conundrums
- Chronic disease states
- The walking, but anxious well
- Happy hypoxics
- Maybe it's COVID-19?

Disaster Role(s) of an EMP: Drug Information

- Drug cures, drugs to avoid
- Drugs to stockpile, don’t stock pile it’s bad
- Reported, perceived, actual, felt at user level shortages

- Med Twitter Ideas, both good and bad
- Literature review and dissemination
- Rumor management and follow up

Disaster Role(s) of an EMP: Regulation

- Rapid changes from the CDC, local, state, and national government
- Protecting yourself & others from health care exposure
- Emergency Medical Treatment & Labor Act (EMTALA)

Disaster Role(s) of an EMP: Operations

- ADC inventories in treatment areas
- Medication preparation at bedside/room
- Inpatient pharmacy delivery facilitation
- Safe drug return to central operations

Disaster Role(s) of an EMP: Problem solving

- Everything takes longer AND keeps changing
- Changes coming from the top down takes time
- Avoiding over use of PPE
- Communication and space issues
- Surges and inventory lag
- Disagreements in care management
- Hard to keep up with information flying around
- Non-adherence to safety practices and protocols
- Recognizing yourself as a non-redundant resource

Disaster Role(s) of a Technician in the ED

Medication Procurement & Preparation Experts

- Emergency kits
- Experts in automated dispending cabinets
- Optimizing ADC par levels
- Shortages and formulary change management
- Best Use Date champions
- Responding to emergency requests

Disaster Role(s) of an EMP: Administration and Medication Management

Administrative

- P.A.C.E planning
- Education
- Policies, guidelines and procedures updates
- Resource management
- Protocol development

UUED COVID-19 AIRWAY MANAGEMENT ALGORITHM

Versopm 4.1 updated 4/10/2020

PREPARATION

Signs of End Organ Damage / Critical Hypoxemia

1) Severe respiratory distress
2) Respiratory Rate >30
3) Altered Mental status
4) Significant increased work of breathing

*02 Sat threshold for intubation is based on provider discretion & may vary by presentation & further data/ experience

** If using HFNC or CPAP: move to negative pressure room or use tent including during transport

***Use CPAP if no HFNC available,

* If utilizing Covid Airway team, alert early to allow time for response and PPE

Location & Patient Selection

- Negative Pressure Room if possible
- If suspected Covid19, consider intubation if patient demonstrates *significant* Hypoxia* ***DESPITE*** Escalating Oxygenation Algorithm (NC @6-10L+ NRB @ 6-10L/min -> HFNC (max 30 L/Min**, 100% FiO2) *or* Low Pressure CPAP (max 6cm H20 in ED***) ***AND***
  - Lack of improvement in clincal status/blood gas after 1hr of Oxygenation **AND/OR**
  - Moderate-Severe respiratory distress **AND/OR**
  - RR>30 **AND/OR** Signs of End Organ Damage

Assemble Team*

- Minimize number of healthcare providers needed to complete procedure safely
- **In-Room (3-4):** 1-2x Attending MD +/- Resident MD or APC, 1x RN, 1 Medic, 1x RT
  - *If resident or APC intubating, Attending MD to run resuscitation from outside room
  - *In-Room team will change with ED P.A.C.E. Surge response
- **Out-of-Room (2-3):** 1x RN (in airbnor PPE); 1x EMT/Runner/PPE monitor, 1x ED PharmD
- Consider CovidAirway team if multiple critical patients or anticipated difficult anatomy

PPE

- Wash or sanitize hands for at least 20 seconds
- All In-Room personnel & RN out-of-Rm must **DON** in order: Goggles + N95 or PAPR --> OR cap --> impermeable gown w/ thumbs through thumb holes --> Inner gloves --> Outer gloves
- **PPE Monitor (EMT):** Supervise all donning and doffing of PPE to ensure no cross contamination

PRE-CHECK and PRE-BRIEF

*HFNC/CPAP criteria
Patient cannot be successfully oxygenated (sats >90% & without resp distress) on 6L NC + NRB

High Flow Nasal Cannula
- Set flow rate to 30 LPM
- Titrate FiO2
- Surgical mask over HFNC
- Encourage incentive spirometry and self proning
-Neg pressure Rm or HEPA Filter

1) CPAP provided via COVID specific set-up V60 CPAP/BiPAP machine with Viral filters in place

2) CPAP via Closed-circ… Mask w/ t-piece viral f…

3) CPAP can be provide… with No mask leak

4) Closed, Neg pressure … or Rm w/ HEPA Filter … place

5) All providers in PAP… erborne precautions

6) Place on CPAP/PSV, … the PSV at 0, dial up PEE… ly if patient's saturations … ot come up with 100% f…

7) Patient must be trans… od with non-aerosolizing tent

Equipment Check

- COVID glidescope is charged & working, all blades, rigid style, & bougie in basket
- Airway Cart w/ Pre-Ox & Intubation Packs stocked & outside of room
- CritCare Cart & US are adequately stocked and located directly outside of room

Pre-Oxygenation Plan

- Position Non-aerosolizing tent over patient, place HOB at 30 deg & Determine optimal pre-oxygenation strategy:
  1) NC @ 10L/min + NRB @ 10L/min **OR**
  2) High-Flow Nasa Cannula w/ Surgical Mask (Max 29L/min)* **OR** Low-Pressure CPAP (max 6cmH20) **OR**
  3) Covid Pre-Oxygenation Kit --> Conver to 2 hand seal w/ jaw thrust Apneic CPAP during apneic period
     Use *MAX FLOW* and *MIN PEEP* needed. Do not bag. Consider NP/Oral airway adjunct

Intubation Plan

Under non-aerosolizing Tent…

- **Plan A:** RSI with VL & preferred blade by most experienced provider. Inflate Cuff ASAP
- **Plan B:** Rescue Oxygenation under plastic sheet --> 2nd attempt VL w/ alternate blade

Rescue Oxygenation options

1) Place SGA w/ viral filter between SGA & BVM
2) Bag w/ BVM w/ viral fitler using *excellent* 2 hand mask seal, & minimal tidal volumes

*NO SURGICAL AIRWAYS

Medication Plan

- **Consider Anxiolytic Dose ketamine**: 20mg IV *slow* push
  - May aid in patient tolerance of pre-oxygenation

*Reserve Ketamine for Asthma/COPD/Agitation

- In-Room: **RS** (see intubation plan dosing chart)
  - *Etomidate* or *Ketamine* *
  - *Rocuronium* or *Succinylcholine*

- In-Room: **Sedation**:
  1) Pre-prime Propofol gtt on pump
  2) Fentanyl gtt
  3) Lorazepam PRN for vent compliance

- Out-of-Room(on standby): **Hemodynamic Suppoet** (*available in Omnicell upon MD request*)
  - Phenylephrine (100mcg/ml) Premade Push-Dose syringe
  - Epinephirne (10mcg/ml) Premade Push-Dose syringe
  - Norepinephrine gtt pre-mixed

UUED COVID-19 Intubation Plan

V4.1 Updated 4/7/2020

Patient Height: ___ Weight: ___ IBW: ___ BMI: ___

Max Personnel in Rm: 4 Recommended ETT Depth: ____

See back of sheet for pre-calculated medication doses* *UU Critical Care Medicine Cards

Height (inches)		Height (cm)	ETT depth
5' 0"	60	152	19
5' 2"	62	157	20
5' 4"	64	163	20
5' 6"	66	168	21
5' 8"	68	173	21
5' 10"	70	178	22
6' 0"	72	183	23
6' 2"	74	188	23
6' 4"	76	193	24

Pre-Oxygenation

#1: COVID Pre-Ox kit (NIPPV mask w/ viral filter & BVM with in-line ETC02 & PEEP valve)

#2: Apneic CPAP w/ excellent two-hand BVM mask seal with filter in place

#3: *Minimal pressure BVM* with excellent two-hand facemask seal w/ viral filter & under plastic drape.

Dose Order	Medication		Notes
	Etomidate	5-40 mg, see dosing chart	Half dose in shock
	Ketamine	1 mg/kg, see dosing chart 20 mg slow IVP for anxiolysis	First line for asthma/COPD/Agitation • Max dose = 200 mg
	Rocuronium	1.2 mg/kg, see dosing chart	Max dose = 100 mg, IBW
	Succinylcholine	1.5 mg/kg, see dosing chart	Max dose = 300 mg
	Push Dose Phenylephrine	100 mcg/mL pre-made syringe	IV push 1-2 mL (100 - 200 mcg)
	Push Dose Epinephrine	10 mcg/mL pre-made syringe	IV push 1-2 mL (10 - 20 mcg)
	Norepinephrine drip	0.01-1 mcg/kg/min	See critical care medication cards

Post Intubation Sedation/Paralysis

Dose Order	Medication		Notes
	Fentanyl drip and boluses	Initial bolus: 50-100 mcg FIRST Infusion: 1 mcg/kg/hr, start rate Bolus: 50-100 mcg q 5min PRN X 3	Use 1st for agitation/vent compliance • S/p 3 boluses, consider rate 25-50 mcg rate increase, max rate or 200 mcg/hr
	Propofol drip and boluses	Infusion: 10-60 mcg/kg/min Bolus: 0.25-0.5 mg/kg	Fent and/or ketamine PRNs prior to rate increase, avoid propofol boluses, if possible
	Ketamine IV push **OR**	0.5-1 mg/kg	May use REMAINDER from intubation vial
	Midazolam IV push **OR**	4 mg IVP q4hr PRN	Vent management or agitation
	Lorazepam IV push	2-4 mg IVP q4hr PRN	Vent management or agitation
	Haldol or Droperidol IVP/IM	Haldol: 5-10 mg Droperidol: 1.25-5 mg	Caution with mult QTc prolonging drugs May repeat X 1
	Vecuronium IV Push	0.1 mg/kg q1hr PRN vent compliance	Max dose = 10 mg, S/p sedation optimized!

Vasopressors

Dose Order	Medication		Notes
	Norepinephrine drip	0.01-1 mcg/kg/min	See critical care medication cards
	Vasopressin	0.04 units/min	Do not titrate
	Epinephrine drip	0.01-1 mcg/kg/min	See critical care medication cards
	Dobutamine	Cardiogenic shock 0.5-20 mcg/kg/min	See critical care medication cards Only AFTER norepi OR epi initiated

Weight (kg)	Weight (lbs)	Etomidate (mg)	Etomidate Half Dose (mg)	Ketamine Induction (1 mg/kg)	Midazolam Induction (0.15 mg/kg)	Midazolam Induction (0.1 mg/kg)	Succinylcholine Paralytic (1.5 mg/kg)	Vecuronium Paralytic (0.2 mg/kg)
40	88	10 mg	5 mg	60 mg	6 mg	4 mg	60 mg	8 mg
45	99	10 mg	5 mg	70 mg	7 mg	4.5 mg	70 mg	9 mg
50	110	15 mg	7.5 mg	75 mg	7.5 mg	5 mg	75 mg	10 mg
55	121	15 mg	7.5 mg	80 mg	8.5 mg	5.5 mg	80 mg	11 mg
60	132	20 mg	10 mg	90 mg	9 mg	6 mg	90 mg	12 mg
65	143	20 mg	10 mg	100 mg	10 mg	6.5 mg	100 mg	13 mg
70	154	20 mg	10 mg	105 mg	▼▼▼	▼▼▼	110 mg	14 mg
75	165	20 mg	10 mg	110 mg			120 mg	15 mg
80	176	20 mg	10 mg	120 mg			120 mg	16 mg
85	187	20 mg	10 mg	130 mg			130 mg	17 mg
90	198	30 mg	15 mg	135 mg			140 mg	18 mg
95	209	30 mg	15 mg	140 mg			140 mg	19 mg
100	220	30 mg	15 mg	150 mg			150 mg	20 mg
105	231	30 mg	15 mg	160 mg			160 mg	▼▼▼
110	242	30 mg	15 mg	165 mg			170 mg	
115	253	30 mg	15 mg	170 mg			170 mg	
120	264	30 mg	15 mg	180 mg			180 mg	
125	275	30 mg	15 mg	190 mg			190 mg	
130	286	30 mg	15 mg	195 mg			190 mg	
135	297	40 mg	20 mg	200 mg			200 mg	
140	308	▼▼▼	▼▼▼	▼▼▼			210 mg (2nd vial)	
145	319						220 mg	
150	330						220 mg	
155	341						230 mg	
160	352						240 mg	
165	363						250 mg	
170	374						250 mg	
175	385						260 mg	
180	396						270 mg	
185	407						280 mg	
190	418						280 mg	
195	429						290 mg	
200	440						300 mg	

Ht	Ht (in)	IBW (kg)	Rocuronium (1.2 mg/kg)	Propofol Induction (1-2 mg/kg)
5'	60	48	50 mg	50-100 mg
5'1"	61	50	60 mg	50-100 mg
5'2"	62	52	60 mg	50-100 mg
5'3"	63	54	65 mg	50-100 mg
5'4"	64	56	65 mg	50-100 mg
5'5"	65	60	70 mg	60-120 mg
5'6"	66	62	70 mg	60-120 mg
5'7"	67	64	75 mg	60-120 mg
5'8"	68	66	80 mg	60-120 mg
5'9"	69	68	80 mg	70-140 mg
5'10"	70	71	85 mg	70-140 mg
5'11"	71	73	85 mg	70-140 mg
6'	72	75	90 mg	70-140 mg
6'1"	73	77	90 mg	80-160 mg
6'2"	74	80	95 mg	80-160 mg
6'3"	75	82	95 mg	80-160 mg
6'4"	76	84	100 mg	80-160 mg
6'5"	77	87	▼▼▼	80-160 mg
6'6"	78	89		80-160 mg
6'7"	79	91		80-160 mg
6'8"	80	94		80-160 mg
6'9"	81	96		100-200 mg
6'10"	82	98		▼▼▼
6'11"	83	100		
7'	84	103		

ED gurney = 74 inches (6'2")
Hospital bed = 82 inches (6'10")

UUED Non-Aerosolizing Tx of Asthma & COPD Exacerbation

Asthma Exacerbation:

Mild

1. Albuterol MDI w/ spacer 4 to 8 puffs q20 min x 3, then q1h PRN + QID scheduled

Moderate

1. Albuterol 4 to 8 puffs w/ spacer q20 min x 3, then q1h PRN + q6h scheduled

Also consider some of all of the below treatments:

2. Epinephrine 0.3 mg IM lateral thigh x, then q5min PRN up to 3 total doses
3. MgSO2 2g IV in 30 mid
4. *If Known Asthmatic*: Dexamethasone 12 mg PO/IM/IV or Solumedrol 125mg IV

Severe

1. Albuterol MDI w/ spacer 4 to 8 puffs q20 min x 3, then q1h PRN + q6h scheduled
2. Epinephrine 0.3 mg IM lateral thigh x, then q5min PRN up to 3 total doses
3. MgSO2 2g IV in 30 min.

   If not responding to above, consider

   a. Ketamine 0.1-0.3 mg/kg slow-push over 3min
   b. Low-Pressure CPAP (max pressure 5mmHg) w/ COVID v60 NIPPV machine
   c. Terbutaline 0.01 mg/kg q 20 min PRN up to 3 doses, max dose 0.25 mg per dose, max of 0.75 mg per 1 hour period
4. *If Known Asthmatic*: Dexamethasone 12 mg PO/IM/IV or Solumedrol 125mg IV

COPD Exacerbation

Mild/Moderate

1. Albuterol MDI w/ spacer 4 to 8 puffs q20 min x 3, then q1h PRN + q6h sched
2. Azithromycin 500mg IV
3. If known COPD → Dexamethasone 12 mg PO/IM/IV or Solumedrol 125mg IV

Severe

1. Albuterol MDI w/ spacer 4 to 8 puffs q20 min x 3, then q1h PRN + q6h sched
2. Azithromycin 500mg IV
3. **If neg pressure room:* Low-Pressure CPAP (max pressure 5mmHg) w/ COVID v60 NIPPV machine
4. **If known COPD* → Dexamethasone 12 mg PO/IM/IV or Solumedrol 125mg IV

*No in-line nebulizers in ED (RT can provide in-line nebs to intubated patient in ICU neg-pressure room

V 4.1 Updated 4/9/2020

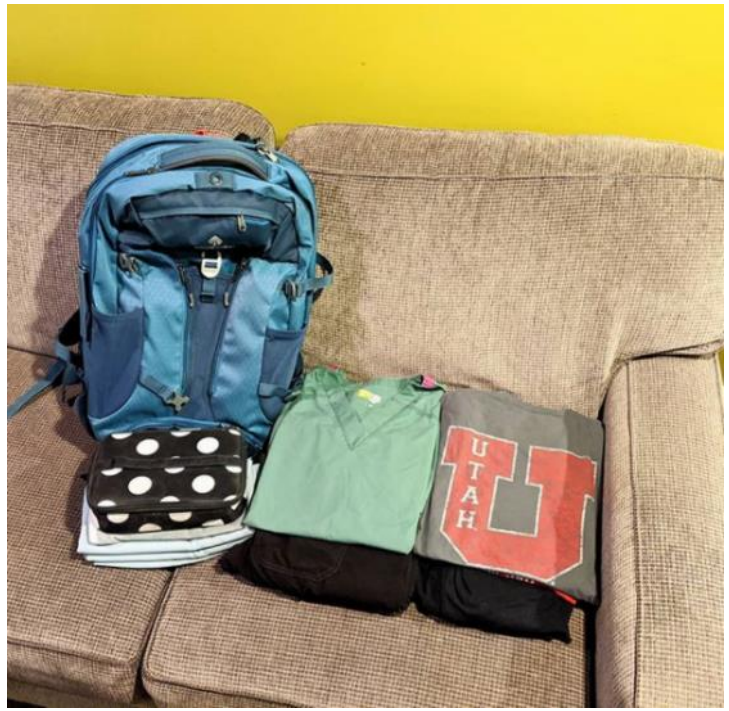
The ED intubation and airway management protocol went through 4.1! reiterations to keep up with changes, drug stock and expert suggestions.

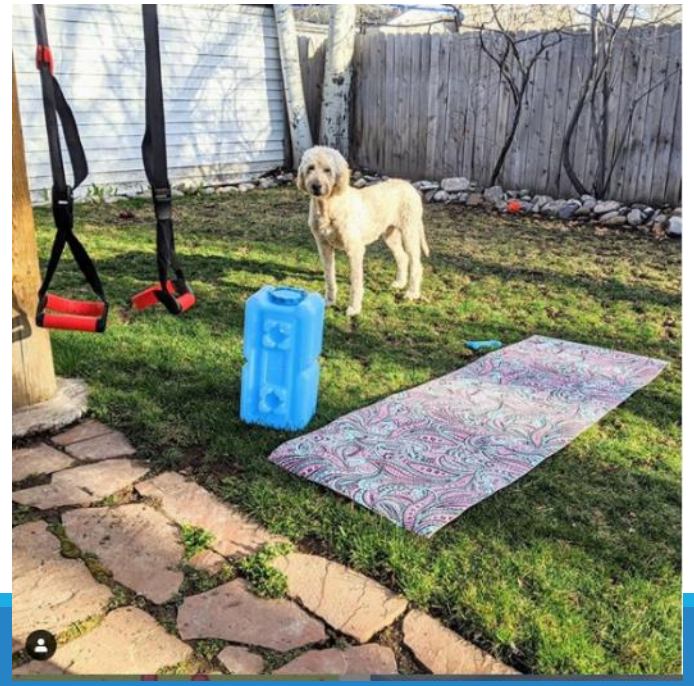
Tips and Tricks

- Have a working understanding of the local, state, and federal response and command systems
- Living communication tools
- Did I hear you say a drug name or “pharmacy”?
- A “no” today does not mean “no” tomorrow
- Back up plans, don’t be afraid to be creative
- Don’t over extend yourself or your team

Tips and Tricks

- Have your own emergency kit, snacks, comfort items, and sleeping needs
- Have a robust phone # list
- Maintain physical and mental health
- Obtain your own PPE if needed
- Phone charger, battery bank
- Find a quiet place and mantras
- Timer for cleaning
- Support team
- Make friends with ambiguity





Test Questions

- Which of the following roles in action should an EM pharmacist not participate in during a pandemic?
  - A) Creating tools for fast decision making and dosing by nursing staff?
  - B) Daily literature upload and dissemination
  - C) Patient care like drug-disease interaction and error prevention
  - D) Daily routine, keep the status quo
  - E) Collaborate with operations for ADC optimization

Test Questions

- Why is yesterday's brand new standard operating procedure (SOP) changed today already?
  - A) Drug formulation shortage announced overnight
  - B) Clinical practice for best care supports research or use of a new drug
  - C) Key personnel are now out on leave due to quarantine
  - D) Best Use Date allows for best inventory use
  - E) All or any of the above, because disasters aren't predictable and we made the best SOP with the knowledge we had yesterday. Today's a new day!

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USHP

COVID-19 Medication Controversies:
-Do you have an ACE (*Inhibitor*) up your sleeve?
-WHO said WHAT? Some things better left *NSAID*

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Disclosure

Instructions:

No relevant relationships or conflicts of interest, financial or otherwise, to disclose

We will discuss off-label use(s) of medications

Learning Objectives

At the conclusion of this activity, ***pharmacists*** should be able to successfully:

1. **Evaluate available literature regarding risks and/or benefits of ACE-I, ARB, NSAID use during an acute COVID-19 infection**

2. **Formulate a recommendation based on available literature when discussing the ACE-I/ARB/NSAID conundrum with providers and patients**

Learning Objectives

At the conclusion of this activity, ***pharmacy technicians*** should be able to successfully:

1. **List medications in the ACE-I, ARB, and NSAID class of medications**

2. **Identify patients who may have concerns regarding continued use of ACE-I, ARB, and NSAID during the COVID-19 pandemic**

Road Map

Discuss controversy regarding ACEi (Angiotensin Converting Enzyme – Inhibitor) & ARB (Angiotensin Receptor Blocker) use in COVID-19 patients

Biologic mechanisms and relevant literature for various hypotheses

Current recommendations for patients taking these medications

Repeat for NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)

Touch on other pertinent classes of medications

Controversy! RAS Inhibitor Use During COVID-19

- Lancet publishes correspondence March 11th (updated March 19th): “The expression of ACE2 is substantially increased in patients with type 1 or type 2 diabetes, who are treated with ACEi & ARBs... Consequently, the increased expression of ACE2 would facilitate infection with COVID-19. We therefore hypothesise [sic] that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19.”

- Panic ensues from patients and medical providers hoping to do the right thing in this rapidly emerging situation

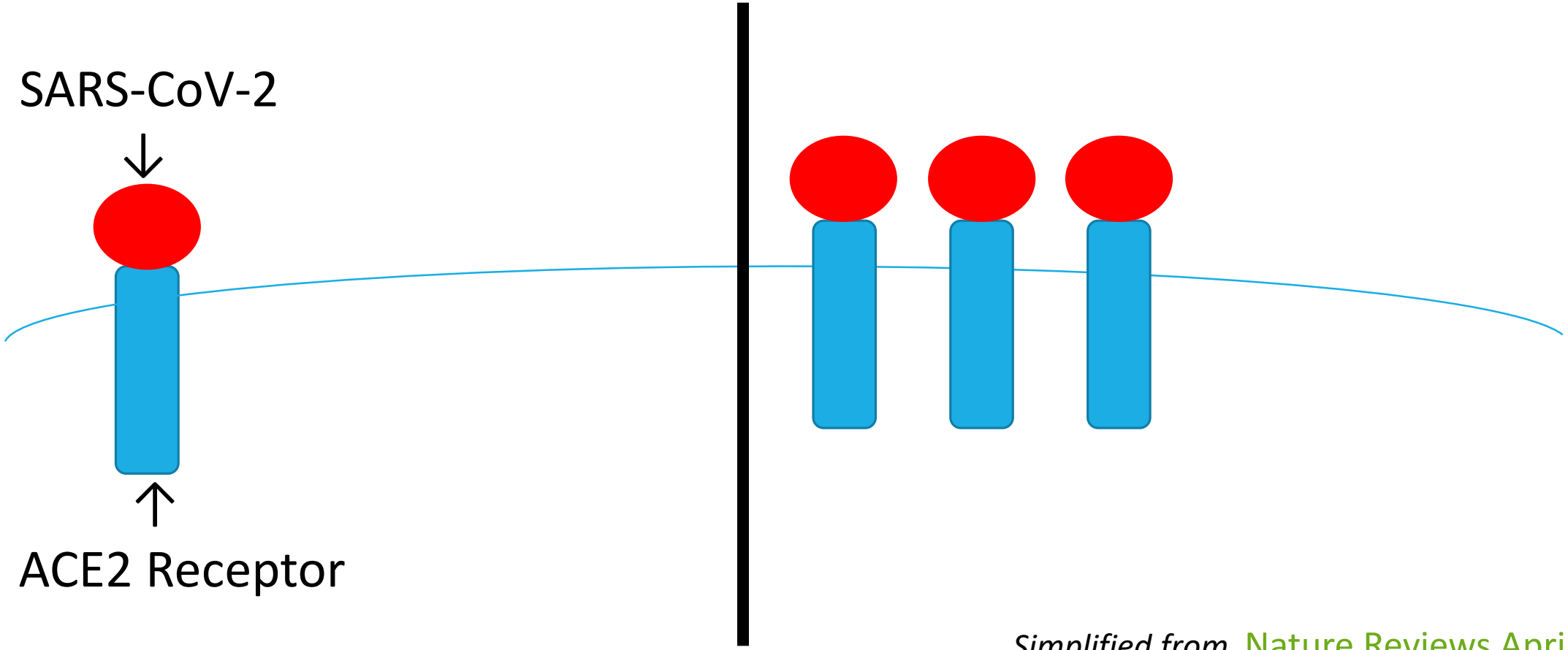
RAS = Renin-Angiotensin System

The Lancet Respiratory Medicine (2020) Link

Hypothesis – RAS Inhibition = Harmful

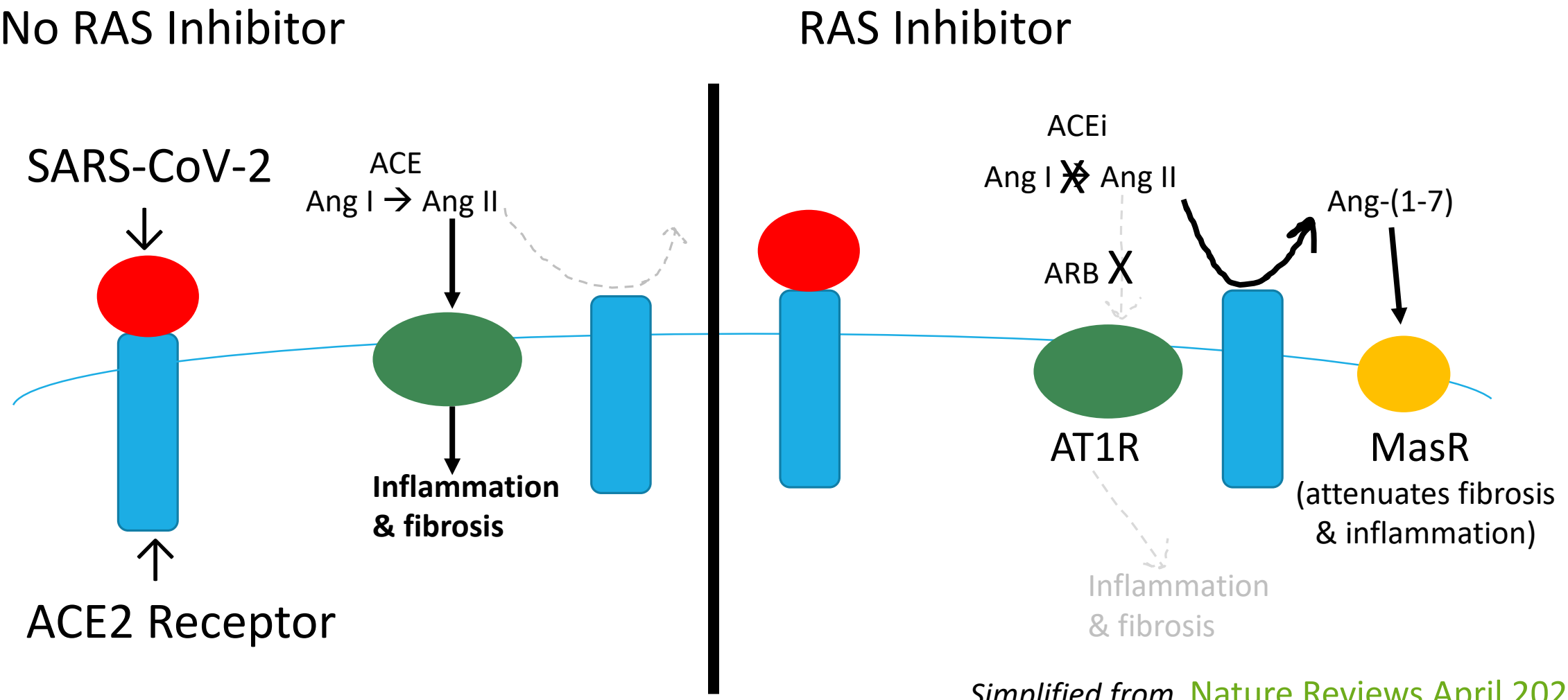
No RAS Inhibitor

RAS Inhibitor



Simplified from Nature Reviews April 2020

Hypothesis – RAS Inhibition = Beneficial



Simplified from Nature Reviews April 2020

ACEi, ARB Use & Confounders?

Perhaps the issue in COVID-19 is not ACEi or ARB use, but potential confounders including increasing age, hypertension (or other underlying indication for ACEi or ARB treatment)

- Many studies have been completed and are ongoing attempting to answer this question
- Nothing conclusive (yet), design limitations, population confounders, when/how to adjust analyses, etc

Should we 'play it safe' and switch patients to another medication for HTN (e.g. amlodipine)?

- Association between RAS Inhibition and COVID-19 remains unknown
- RAS Inhibition affects much more than blood pressure (kidney protective, etc)
- Switching medications may require additional monitoring (difficult whilst physically distancing)
- IF RAS inhibition affects COVID-19, not sure in what direction and how robustly

MA ↓ Mortality – Hypertension Aug 2020

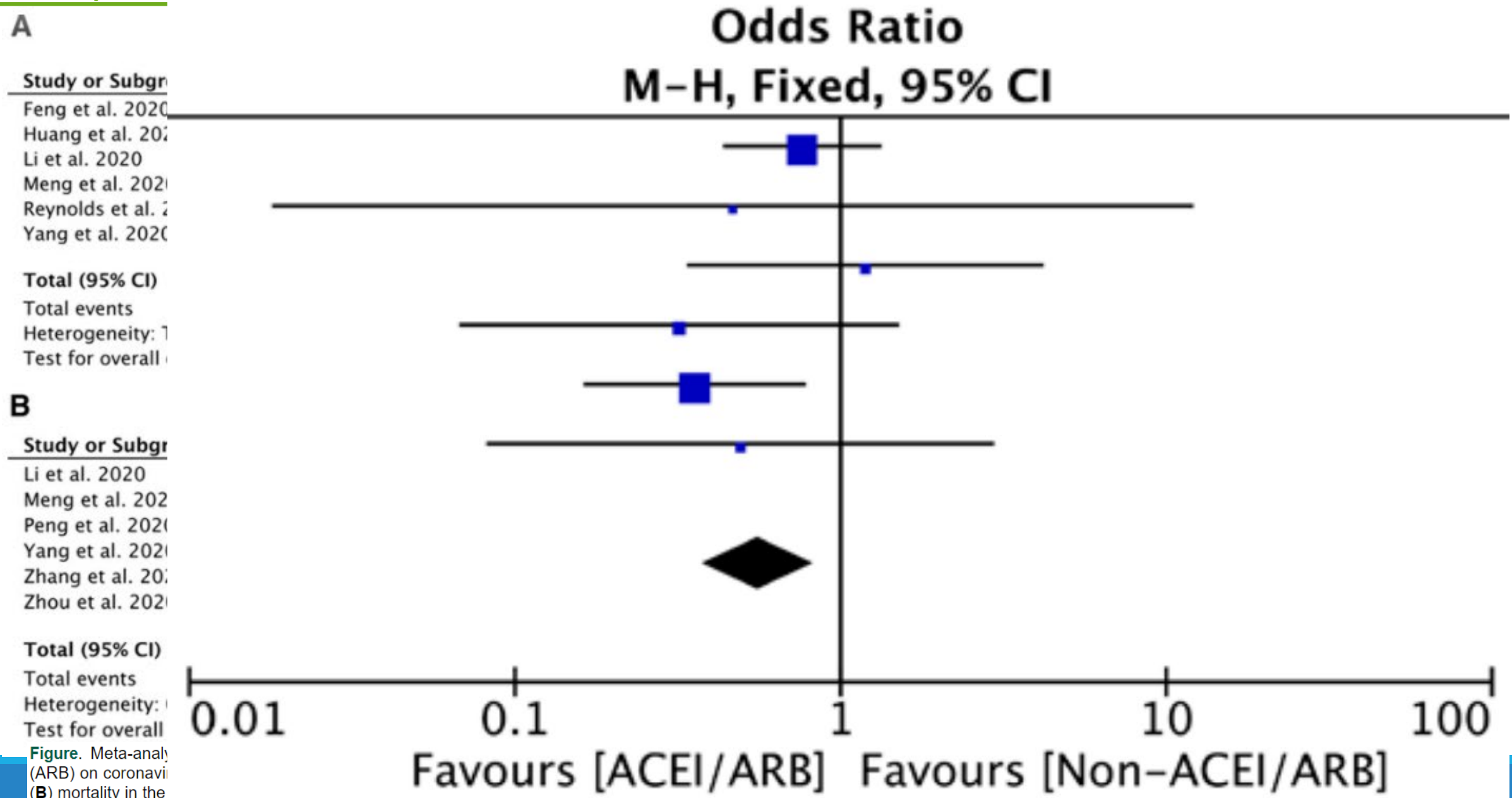


Figure. Meta-analy
(ARB) on coronavi
(**B**) mortality in the
M-H indicates Mantel-Haenszel.

SR & MA, n > 28k: *Current Atherosclerosis Reports Aug 2020*

Studies	Estimate (95% C.I.)	Ev/Trt
Andrea	0.516 (0.209, 1.272)	21/68
Chen	0.414 (0.116, 1.476)	4/32
Feng	0.160 (0.035, 0.724)	2/33
Huang	0.123 (0.014, 1.062)	1/20
Ip	0.707 (0.550, 0.910)	137/46(
Li	0.762 (0.436, 1.333)	21/11
Meng	0.467 (0.018, 12.143)	0/17
Reynolds	0.972 (0.794, 1.190)	252/10
Richardson	1.264 (0.982, 1.627)	130/41
Yang	0.345 (0.109, 1.090)	4/43
Zhang	0.356 (0.163, 0.782)	7/18
Subgroup H (I^2=6728 % , P=0.001)	**0.670 (0.495, 0.908)**	**579/24(**
Bean	0.832 (0.644, 1.074)	127/39
Dauchet	1.597 (0.865, 2.946)	34/62
Guo	2.139 (0.785, 5.828)	7/19
Mancia	0.240 (0.207, 0.279)	258/28
Mehta	1.618 (1.136, 2.304)	47/21
Subgroup T (I^2=9760 % , P=0.000)	**0.980 (0.385, 2.498)**	**473/35**
Overall (I^2=9434 % , P=0.000)	**0.671 (0.435, 1.034)**	**1052/59**

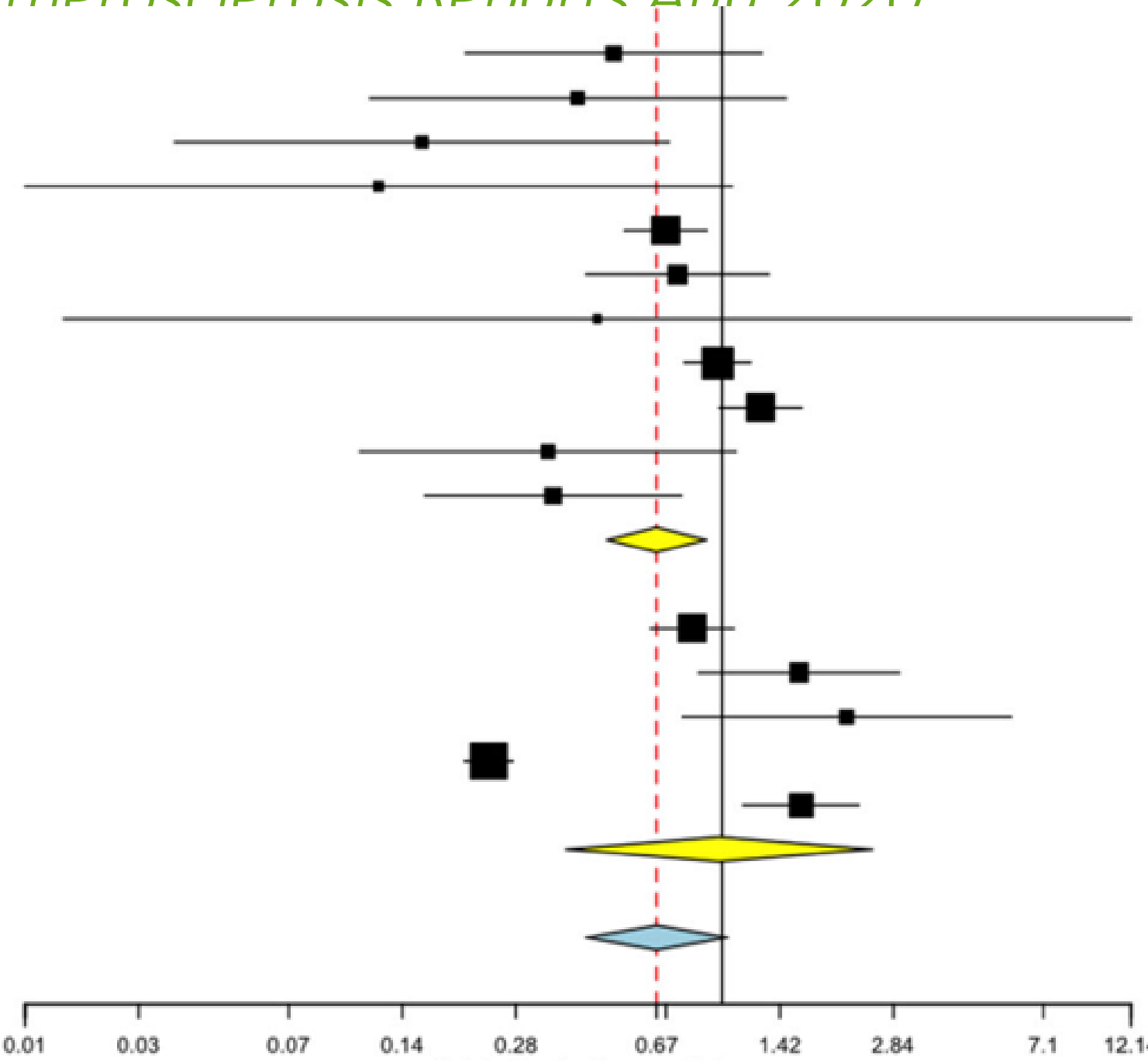
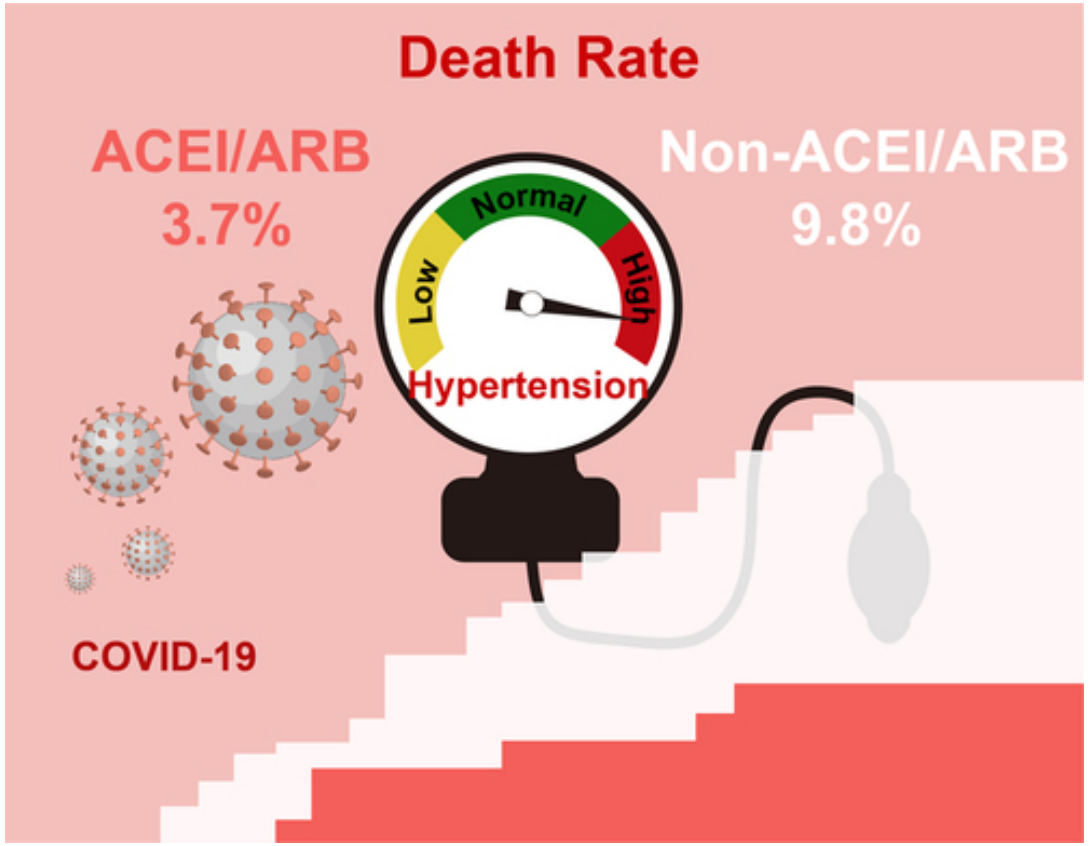


Fig. 1 Subgroup analysis of death/critical events in ACEi/ARB v
ACEi/ARB. Subgroup analysis of death/critical events (OR 0.6
0.435 to 1.034, $p = 0.071$) in sixteen studies with 5996 patie
ACEi/ARB vs 10,103 non-ACEi/ARB patients. Total effe

Dx COVID-19: Continue ACEi or ARB?



- Retrospective, multi-center study including 1128 adult patients w/ hypertension diagnosed with COVID-19, where 188 using ACEI/ARB and 940 not using ACEI/ARB

- Admitted to 9 hospitals in Hubei Province, China from December 31, 2019 to February 20, 2020

- All-cause mortality was lower in the ACEI/ARB group versus the non-ACEI/ARB group (adjusted hazard ratio, 0.42 [95% CI, 0.19–0.92]; *P*=0.03)

- Subgroup compared use of other antihypertensive meds, ACEI/ARB associated w/ decreased mortality (adjusted hazard ratio, 0.30 [95% CI, 0.12–0.70]; *P*=0.01) in patients with COVID-19 and coexisting hypertension

Zhang, et al Circulation Research June 2020, Graphic Abstract

Link to ACC Summary (April 24, 2020)

Dx COVID-19: Continue ACEi or ARB?

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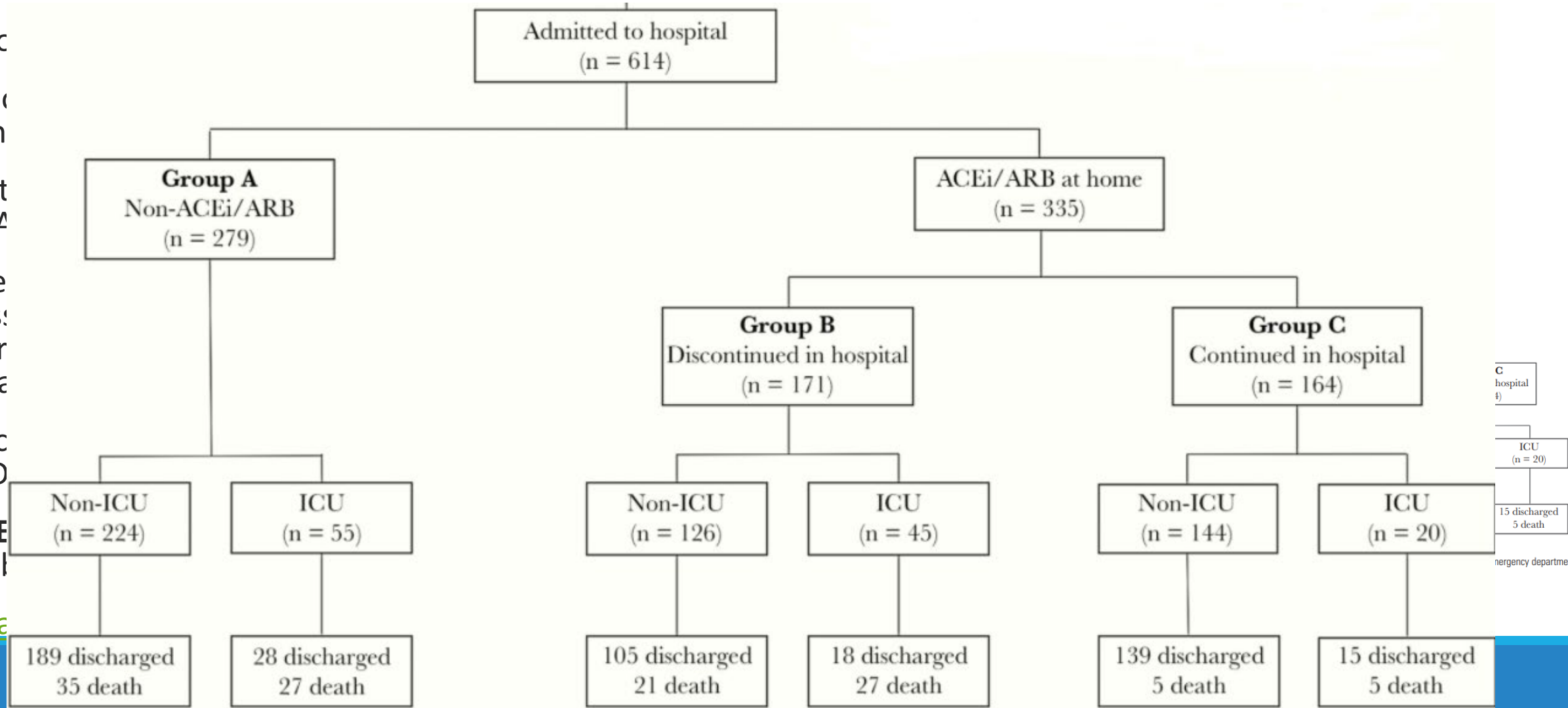


“Interim” Final Word

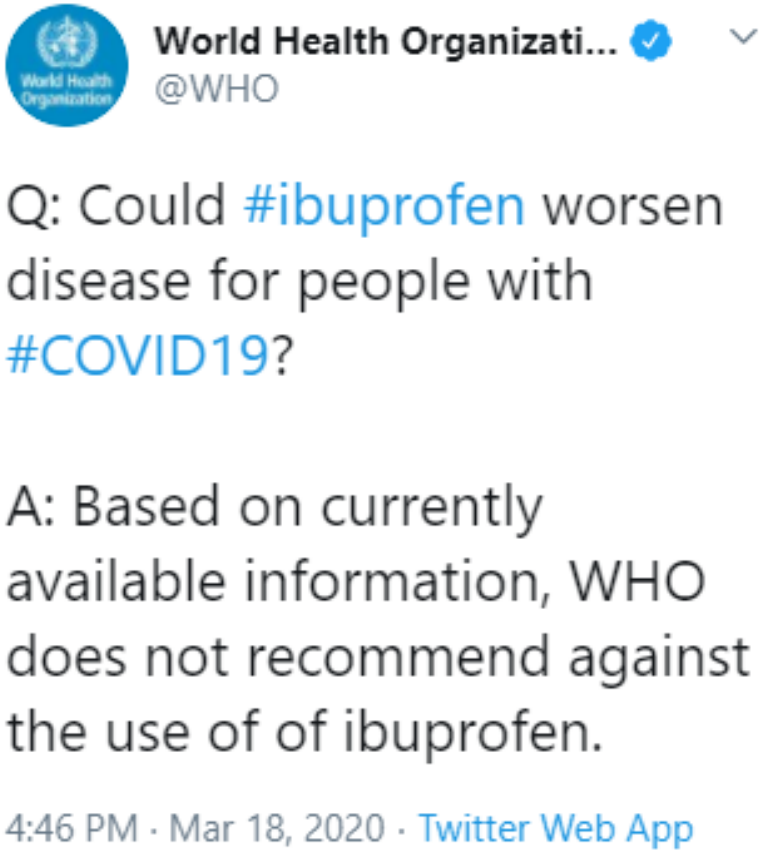
Recommend / Strongly Encourage (and many other synonyms) continuing ACEi/ARB treatment.

Not just my opinion…

American College of Physicians, American Heart Association, American College of Cardiology, European Society of Hypertension, ESC Council on Hypertension, and many others.

American Diabetes Association didn’t have an official statement I was able to find, but publications in their society journal were congruent with the recommendation to continue treatment with an ACEi/ARB or other cardiovascular/diabetes medication that has been implicated with increased ACE2 expression

Controversy! NSAID Use During COVID-19



- Lancet publishes letter March 11th (updated March 19th): "ACE2 can also be increased by thiazolidinediones and ibuprofen… We therefore hypothesise [sic] that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19."

- March 14th French Minister of Health recommends against anti-inflammatory medications (e.g. ibuprofen, cortisone) and in the event of fever recommends taking acetaminophen (paracetamol) via Tweet

- March 18th WHO 'clarifies' stance via Tweet, "WHO does not recommend against the use of ibuprofen"

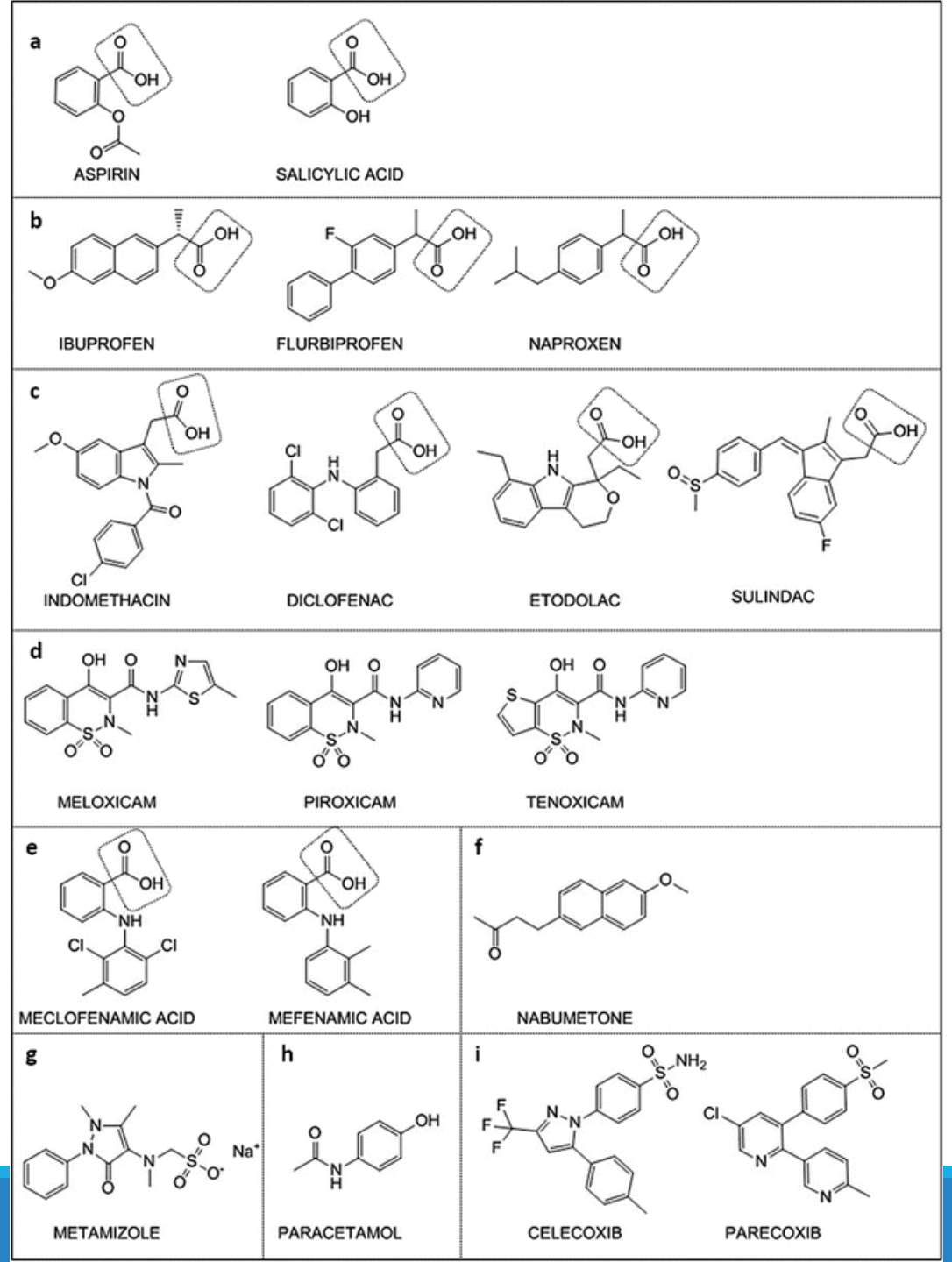
The Lancet Respiratory Medicine (2020) Link

NSAID Use Caveats

This question does not have the same level of evidence as the previous therapeutic conundrum (ACEi/ARB). Much of this section is based on hypotheses, broad derivations and outright speculation. It is also more difficult to study as Over-The-Counter use makes it hard to establish usage. Not to mention individual patient dosing can vary widely, as anyone performing medication histories can attest

NSAIDs are much broader from a chemical structure standpoint (e.g. COX 1 & COX 2 inhibition differences, varying prostaglandin effects, PK parameters) relative to other medication classes discussed in the context of COVID-19 controversy; some differences may yet be elucidated.

E.g. certain NSAIDs *may* be harmful while others may be equivocal or beneficial.



Chemistry, Pharmacodynamics, and Pharmacokinetics of NSAIDs 2016

Why Might NSAIDs be Harmful?

- Ibuprofen upregulates ACE2, potentially increasing viral load and/or likelihood SARS-COV-2 enters cells via increased chances to bind ACE2

- In bacterial soft tissue infections, patients on NSAIDs experienced more severe infections, thought to be due to either immune-depressive effects or initial symptom suppression resulting in delayed treatment initiation

- Fever is a natural physiologic response to viral infection and reduces viral activity; antipyretics, such as NSAIDs, could reduce the body's natural defense systems against viruses

- Centre for EBM notes, "NSAIDs do not significantly reduce total symptoms or duration of illness in Acute Respiratory Infections." **Note**: this summary was not looking at COVID-19 respiratory infections specifically [March 24th 2020 Link]

- NSAIDs worsen hypertension and other disease states, which *may* make patients more susceptible to severe COVID-19 infections compared to their baseline risk

Drug Safety June 2020

Why Might NSAIDs be Beneficial?

Or at least not as harmful as initially thought

- Ibuprofen upregulating ACE2 enzyme was found in a single study in diabetic rats; perhaps more robust evidence is needed in this area. Its unclear how long NSAIDs would need to be taken before upregulation of ACE2 would occur in humans, if at all. Not to mention ACE2 upregulation has not been linked to worse outcomes in COVID19 (see ACEi/ARB section)

- NSAIDs masking symptoms would be unlikely to cause problems as widespread and robust treatments of COVID-19 are currently lacking; wouldn't be appreciably delaying treatment as there are no time-sensitive outpatient therapies to start at present*

- As the sequelae of COVID-19 severe respiratory infections are still being elucidated, perhaps the immune-depressive effects of NSAIDs may be helpful (akin to corticosteroid use)

- If antipyretic therapy is harmful to patients with COVID-19 than acetaminophen (paracetamol) would also be detrimental. I was unable to find any evidence that acetaminophen is harmful to COVID-19 patients*

- Mortality from COVID-19 may be worsened during 'surges' so if an NSAID is able to keep patients out of the hospital that *may* have downstream benefits

Drug Safety June 2020

*Note this may change during the time between the slide preparation and presentation

NSAID Literature

- Much of it derived from respiratory infections in general, not specifically COVID-19

- Naproxen as part of a medication cocktail was effective in treating Influenza A (H3N2) Link

- Recent systematic review of six clinical trials (included study above) recommends caution until more data are available; the authors suggest naproxen may be a good choice for future study Link

- LIBERATE trial is underway looking at ibuprofen as a potential treatment for COVID-19 and reduction of lung injury in acute hypoxemic respiratory failure lipid ibuprofen NCT04334629

- Case-control survey study underway: Role of Ibuprofen and Other Medicines on Severity of Coronavirus Disease 2019 (RISC) NCT04383899

What's Your Recommendation

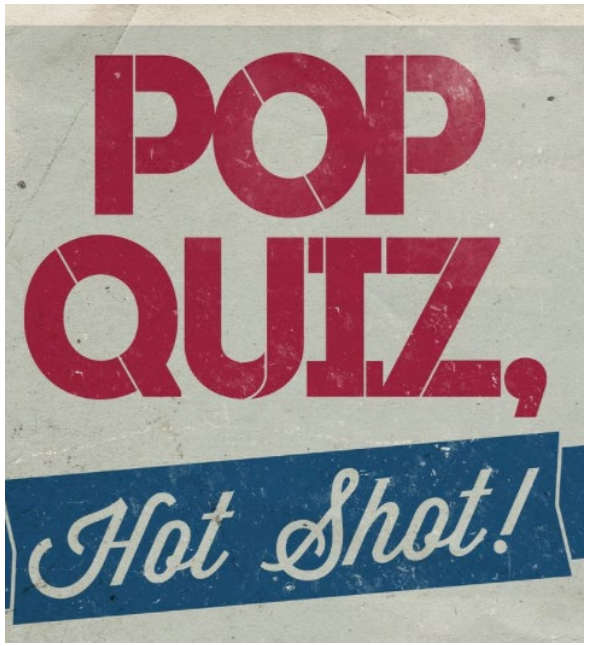
- Assess indication and potential benefits of NSAID treatment

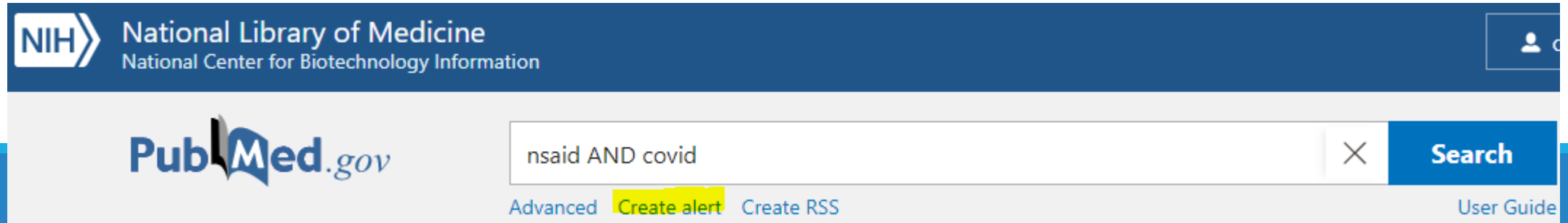
- **IF** decision is made to treat with NSAIDs use the lowest effective dose for the shortest duration

- Anecdotally, many providers and patients do not fully grasp the NSAID Ceiling Effect (well shown in analgesia studies); "There are only so many COX *enzymes* to block"

- Assess for comorbidities and the possibility of NSAIDs exacerbating those conditions

- Continue to watch for new publications
Pro-tip: Create alert(s) in NCBI's PubMed - must be signed in

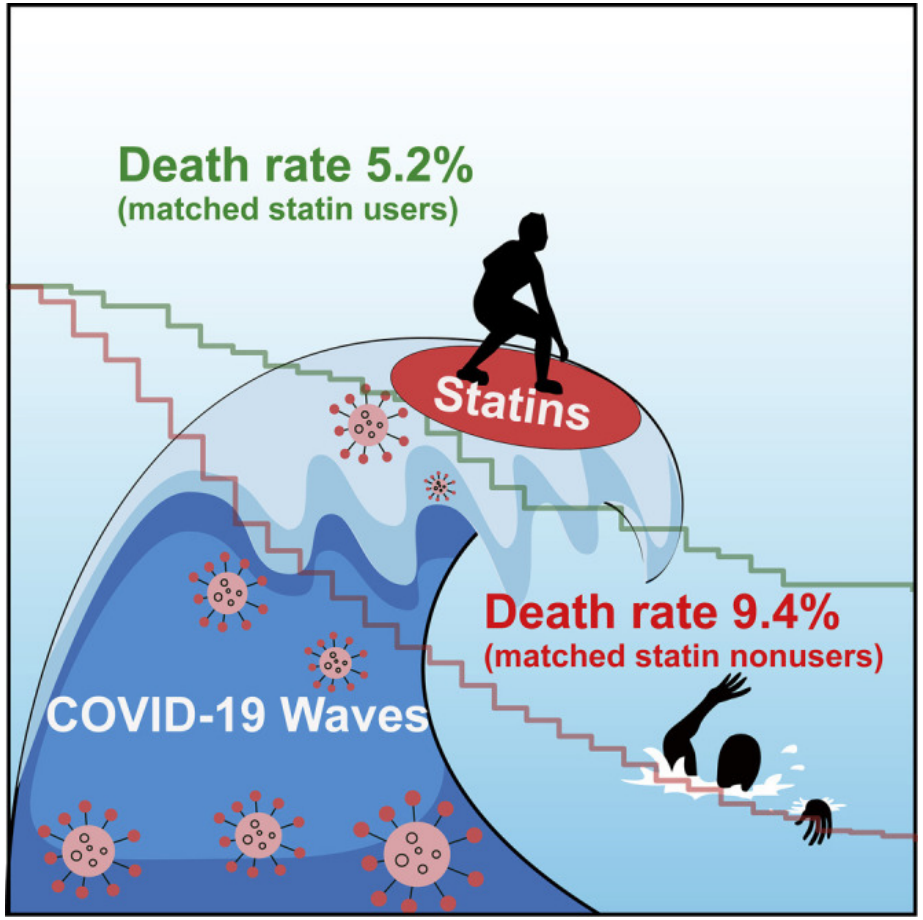




What about other med classes?

Due to time constraints and limited data relative to ACE-I, ARB and NSAID use we will not dive deep into these classes today

- **Thiazolidinediones (TZDs)**
  - Potentially useful? Link → Med Hypotheses July 2020
  - Harmful? (upregulates ACE2 in Rats): → Sci World J 2014
- **HMG-CoA Reductase Inhibitors (Statins)**
  - ↓ Risk of mortality: Link → Cell Metab Aug 2020
- **Proton Pump Inhibitors (PPIs)**
  - ↑ Risk of severe clinical outcomes: Link → Gut July 2020



Graphical Abstract, Cell Metab Aug 2020

Questions, Discussion

Test Questions

T/F: There exists clear and convincing evidence regarding which medications should be discontinued if a patient is at all concerned about COVID19

A. True

B. False

Test Questions

MC: Which of the following medications has not been subject to controversy in patients infected with COVID19

A. Ibuprofen

B. Telmisartan

C. Docusate

D. Lisinopril

Coagulopathies in COVID

Laura Steffens, PharmD, BCCCP, MS
September 12, 2020
USHP Winter Meeting

IMPLICATIONS FOR VTE PROPHYLAXIS AND TREATMENT

Disclosure

Relevant Financial Conflicts of Interest

- The presenter, Laura Steffens, has no financial conflicts of interest to disclose.

Off-Label Uses of Medications

- The use of tPa for empiric treatment of microthrombi associated with COVID will be discussed.

Learning Objectives

Pharmacists

- Describe coagulopathies associated with COVID infections and apply guideline recommendations for venous thromboembolism (VTE) prophylaxis and treatment.

Technicians

- Distinguish between oral, intravenous (IV), and subcutaneous (SQ) medications for VTE prophylaxis and treatment.

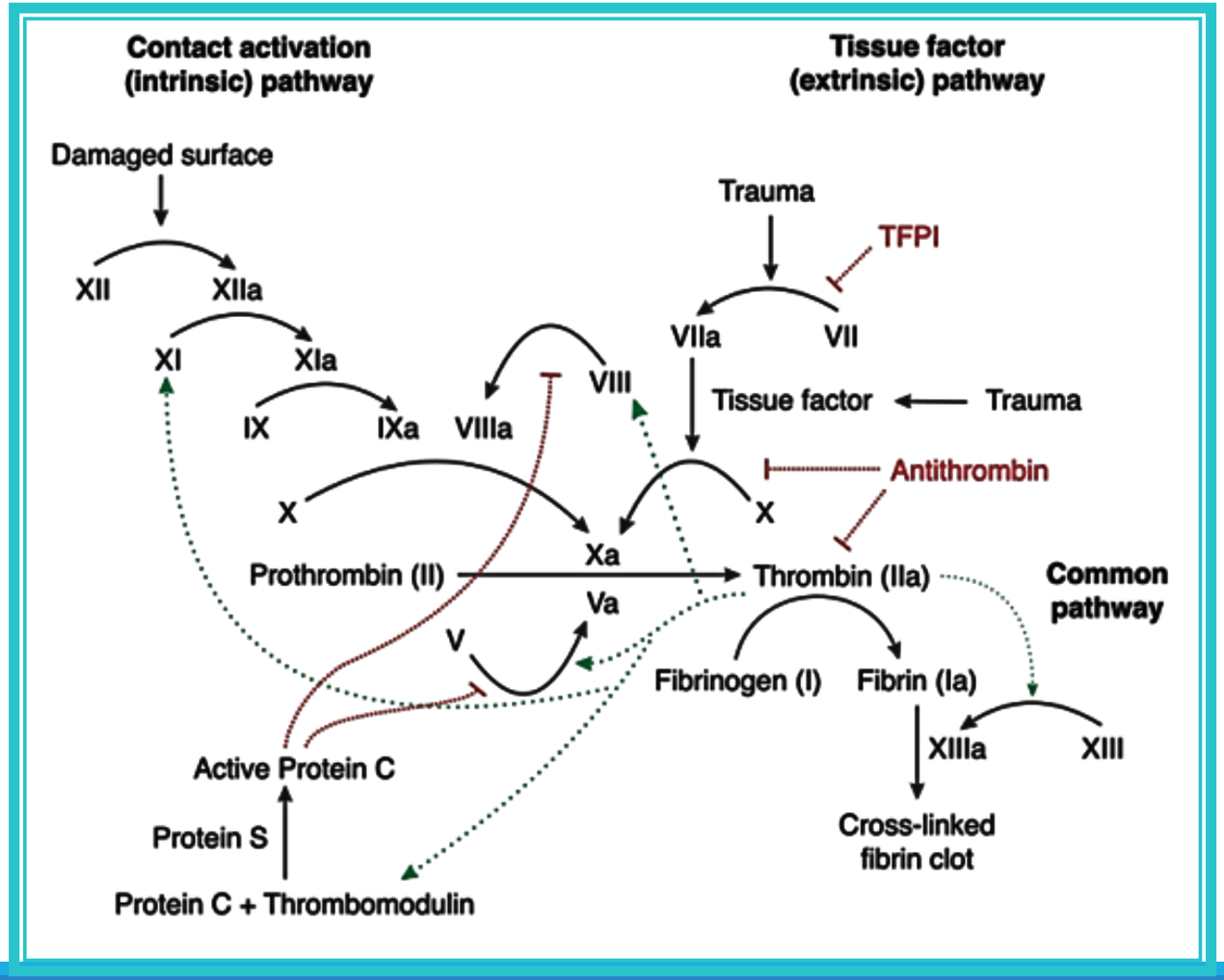
Background

- High risk for VTE development in COVID (+) admitted to a hospital
- Similar coagulopathy pattern as seen in SARS and MERS
- Incidence of VTE 1.1-69% in COVID patients
- Higher morbidity and mortality in those who develop VTE
- Practicality of diagnosis can be challenging

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
COVID-19 and VTE/anticoagulation: FAQ. https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation. Accessed online 8/13/2020, last updated 7/20/2020

Pathophysiology

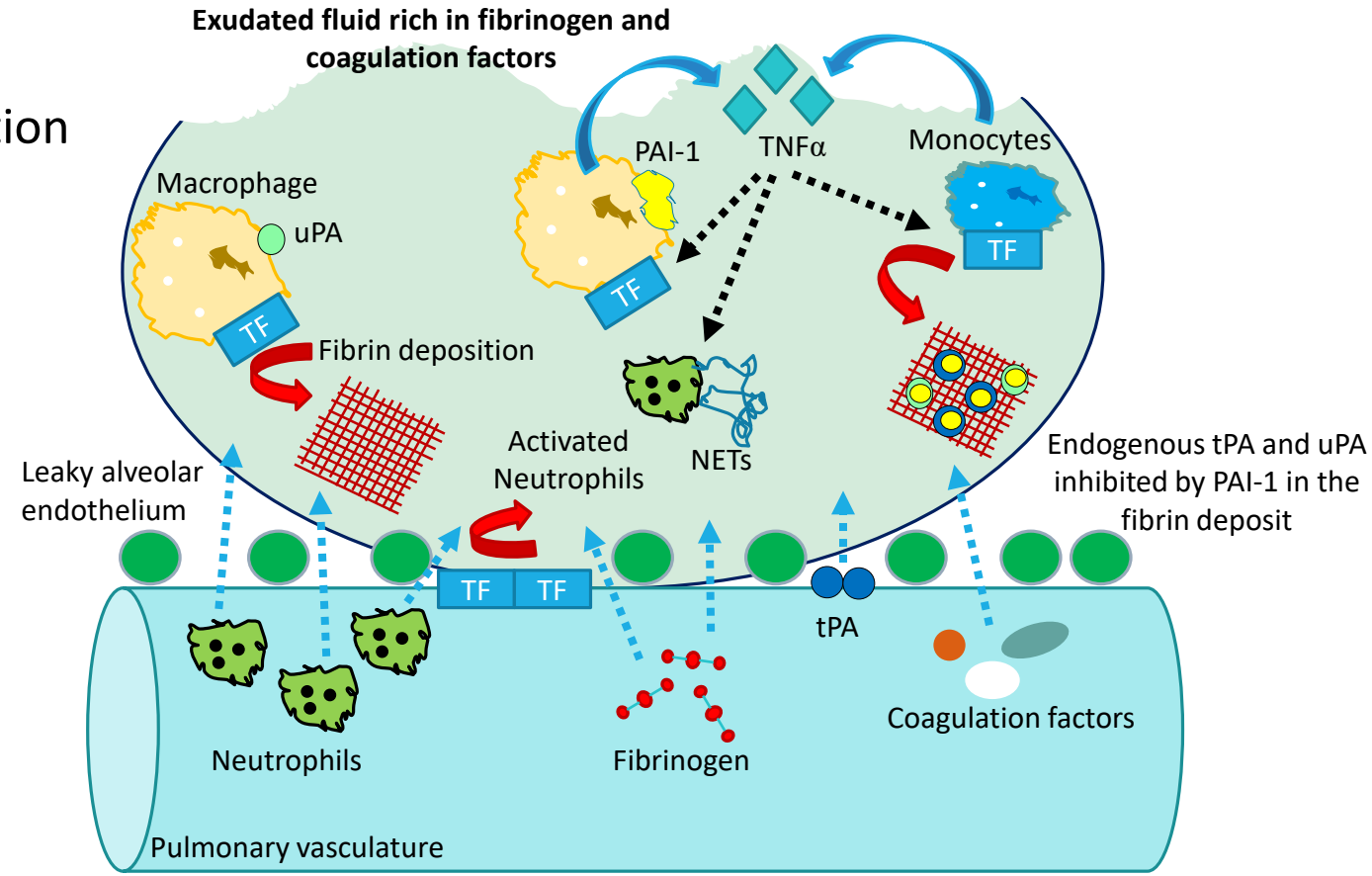
Coagulation Cascade Review



Joe D. Coagulation full. https://commons.wikimedia.org/wiki/File:Coagulation_full.svg (open access). Updated 4/22/07. Accessed 8/23/2020.

Coagulopathy in ARDS

- Permeability of alveolar-capillary junction
- Infiltration of various inflammatory and coagulation factors
- Tissue factor exposed on damaged epithelium
- Increased production of fibrinogen
- Increased PAI-1 release (hypofibrinolytic state)
- Unrestricted inflammation and fibrin deposits
- High risk for clot development
- Concern in later stages for mass fibrin deposits



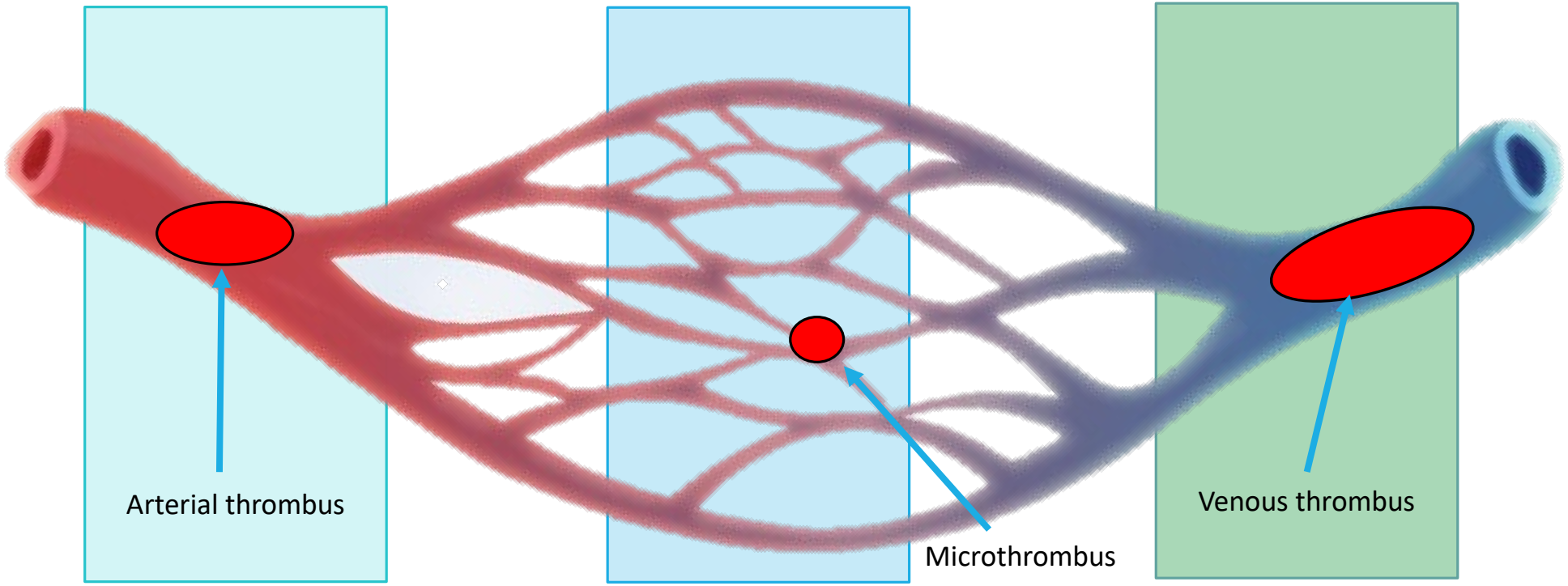
Maldonado E, et al. *J Gen Intern Med* 2020; 1-9: doi:10.1007/s11606-020-05906-y.
Whyte CS, Morrow GB, Mitchell JL, et al. *J Thromb Haemost* 2020 [ePub ahead of print]. PMID: 32329246.

Various Thrombi Formations

Stroke, acute coronary syndrome
- Antiphospholipid antibodies?
- Platelet activation
- Increased fibrinogen

Localized intravascular Coagulation
- Activated coagulation
- Leukocyte activation
- Endothelial damage

Venous Thromboembolism
- Increased fibrinogen and factor VIII
- Activated coagulation
- Enhanced platelet-vessel wall interaction

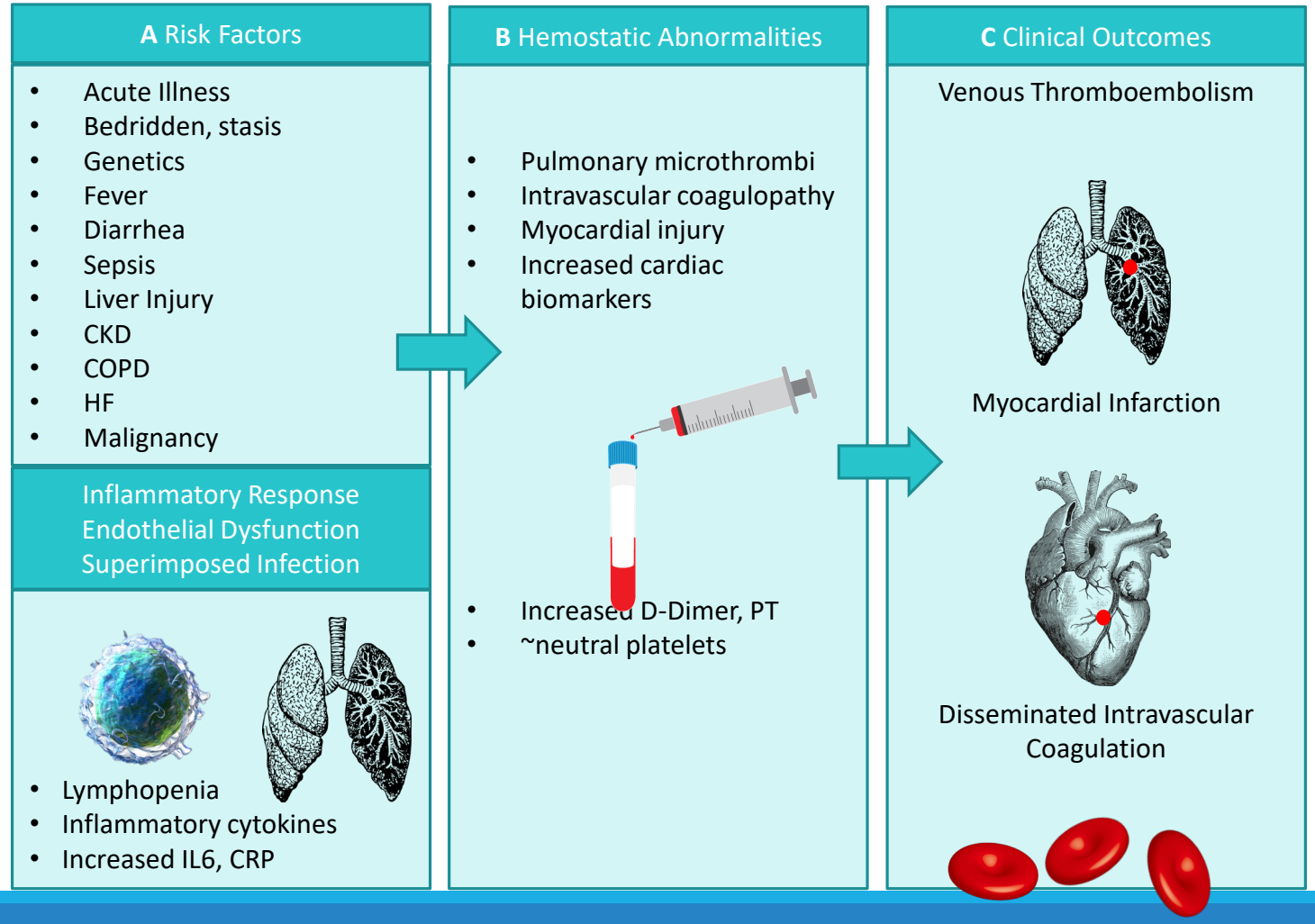


Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Iba T. et al. *Crit Care Med* 2020; Volume online first issue: doi: 10.1097/CCM.0000000000004458.
Community Emergency Response Team. Capillary system. https://commons.wikimedia.org/wiki/File:Capillary_system_CERT.jpg. Updated November 2013, Accessed 8/23/2020.

Overall Effects

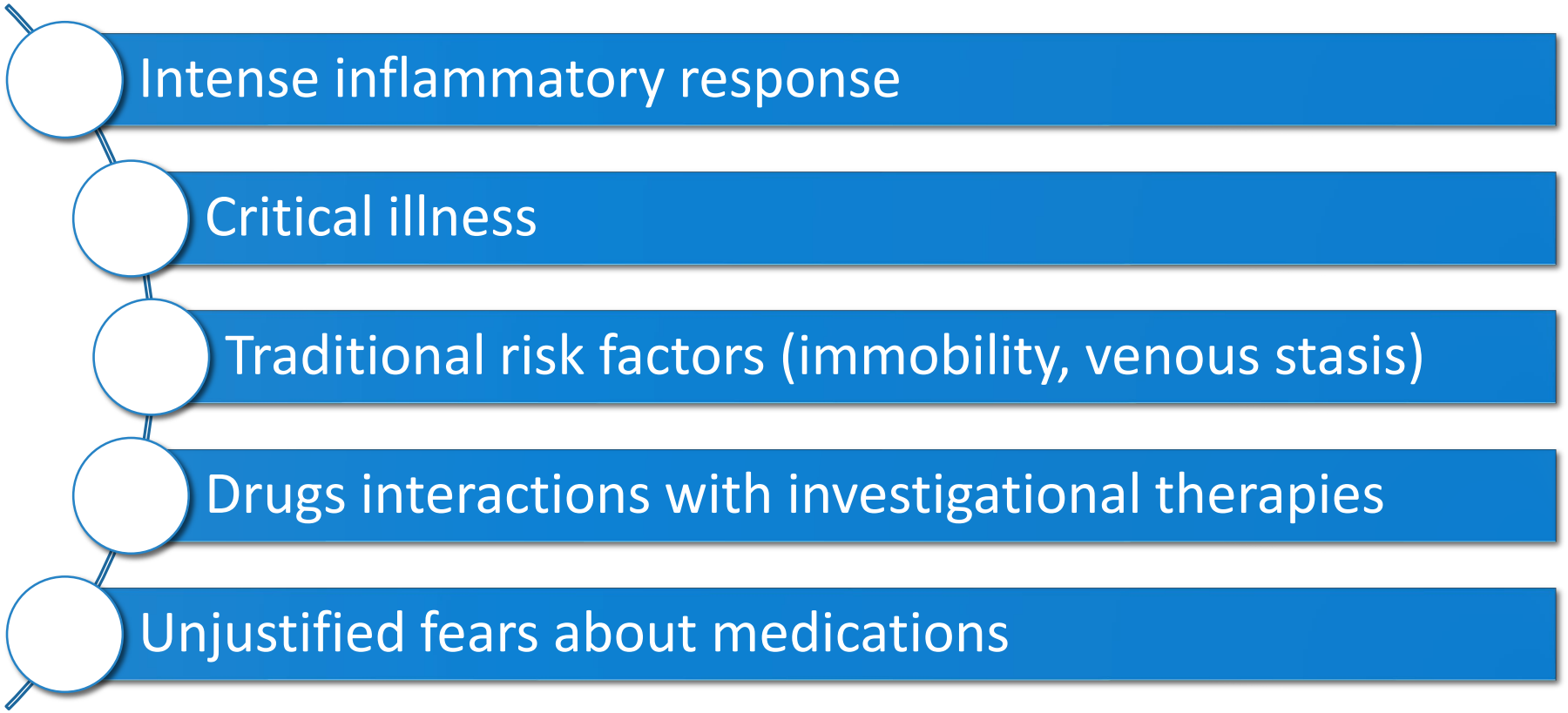
Of note, uncommon to see:

- Thrombocytopenia
- Hemolytic anemia



Pixabay. COVID. https://pixabay.com/. Updated 2020. Accessed 8/23/2020.
Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Iba T. et al. *Crit Care Med* 2020; Volume online first issue: doi: 10.1097/CCM.0000000000004458.

Additional Risk Factors



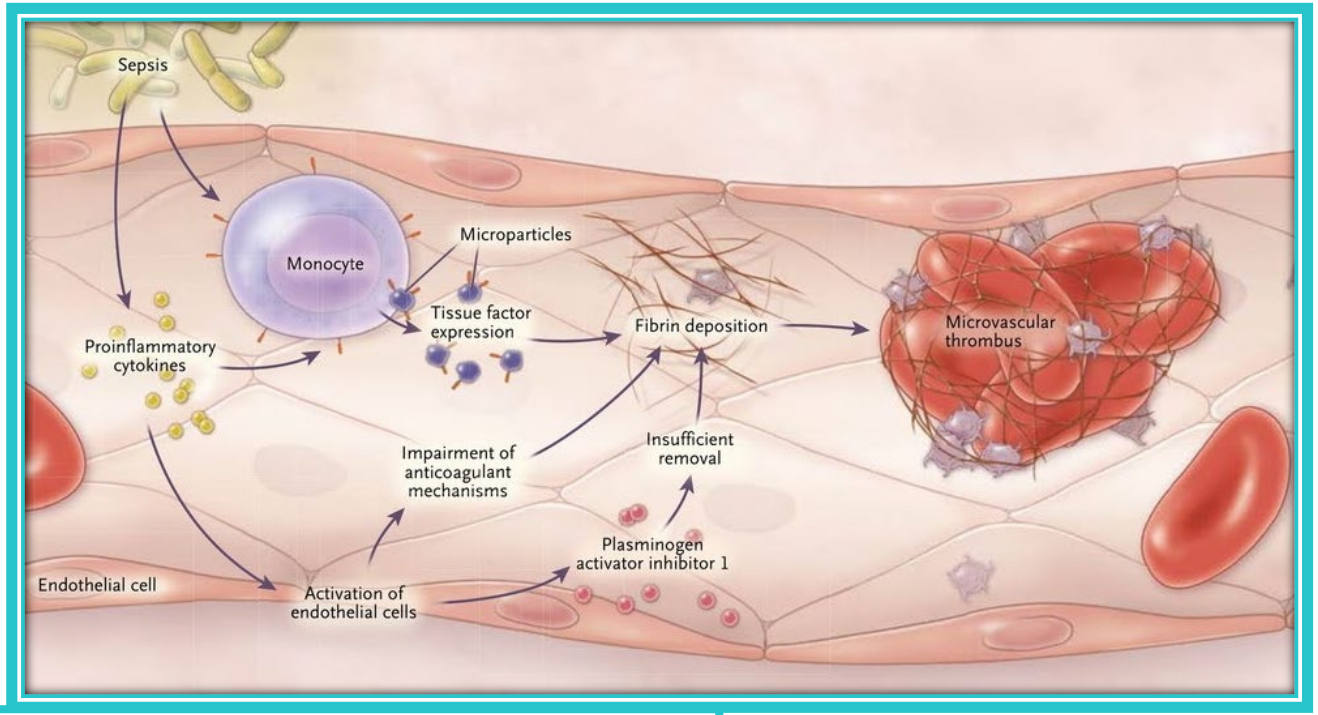
Progression of Disease and Coagulopathy

Disseminated intravascular coagulation

Consumptive coagulopathy

Lab characteristics

- PT ⬆
- PTT ⬆
- Fibrinogen ⬇
- D-dimer ⬆
- Red cells – schistocytes



Single center study in China (N=183)

- 71% of those who died developed DIC
- 0.6% of those who lived developed DIC

Tang N, et al. *J Thromb Haemost* 2020;18:844-847.

Implications for Prevention and Treatment

Medication	Mechanism of Action	Typical Doses
Unfractionated Heparin (UFH)	• Enhances action of anti-thrombin III to inactive thrombin, Factor Xa, and other clotting factors • *Neutralizes procoagulable factors to protect endothelial cells, maintain tight junctions, and minimize edema and leakage, particularly related to COVID* • *Potential anti-inflammatory effects*	Prophylaxis: 5000-7500 units SQ Q8-12 h Treatment: 80 units/kg bolus, 18 units/kg/hr IV, or other variations
Low Molecular Weight Heparin (LMWH)	• Same as UFH, but higher affinity for Factor Xa • *Same postulated benefits in COVID as UFH*	Prophylaxis: 40 mg daily, 30 mg BID SQ Treatment: 1 mg/kg BID SQ **Adjusted for renal function*
Fondaparinux	• Binds antithrombin III to specifically inhibit Factor Xa • *Unknown supplemental benefits in COVID at this time or if confers the benefits as UFH and LMWH*	Prophylaxis: 2.5 mg daily SQ Treatment: 5-10 mg per day SQ (weight-based) **Adjusted for renal function*

Implications for Prevention and Treatment

Medication	Mechanism of Action	Typical Doses
Warfarin	• Inhibition of vitamin K activation, which is required for synthesis of clotting factors II, VII, IX, and X • *Unknown supplemental benefits in COVID at this time*	Varies, but typical starting dose of 5 mg daily PO Adjust with INR
DOACs (Rivaroxaban, Apixaban)	• Direct inhibition of Factor Xa • *Unknown supplemental benefits in COVID at this time*	Varies with each oral agent **Adjusted for renal function*
Tissue plasminogen activator (tPA)	• Converts plasminogen to plasmin to break down fibrin • *Postulated benefit during increased PAI-1 release (hypofibrinolytic state) during active COVID infection*	Typically 50-100 mg IV over various times, usually 2 hours Can be given as catheter-directed therapy

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Iba T. et al. *Crit Care Med* 2020; Volume online first issue: doi: 10.1097/CCM.0000000000004458.

Question 1

Which of the following medications do not currently have additional postulated benefits beyond prevention of VTE in COVID positive patients admitted to the hospital?

A. Enoxaparin
B. UFH
C. Rivaroxaban
D. tPA

Diagnosis and Estimation of Risk

COVID Lab Value Trends

Lab Value	Effects in COVID	Notes
D-dimer	Elevated	• Higher risk of ICU admission, mechanical ventilation, and/or death • Elevated in high plasmin and fibrinolytic activity (diabetes, cardiovascular disease, hypertension; challenging to attribute solely to clot
PT	Elevated	
PTT	Elevated	• Elevation proposed due to increased factor VIII • Not as elevated relative to PT
Fibrinogen	Elevated	Major roll in DIC development assessment
CRP	Elevated	Augments tissue factor exposure, further promoting coagulopathy
PLT	Neutral to mild decrease	Not usually a significant finding, unless severe illness
IL-6	Elevated	Proinflammatory cytokines leading to further alveolar-capillary permeability

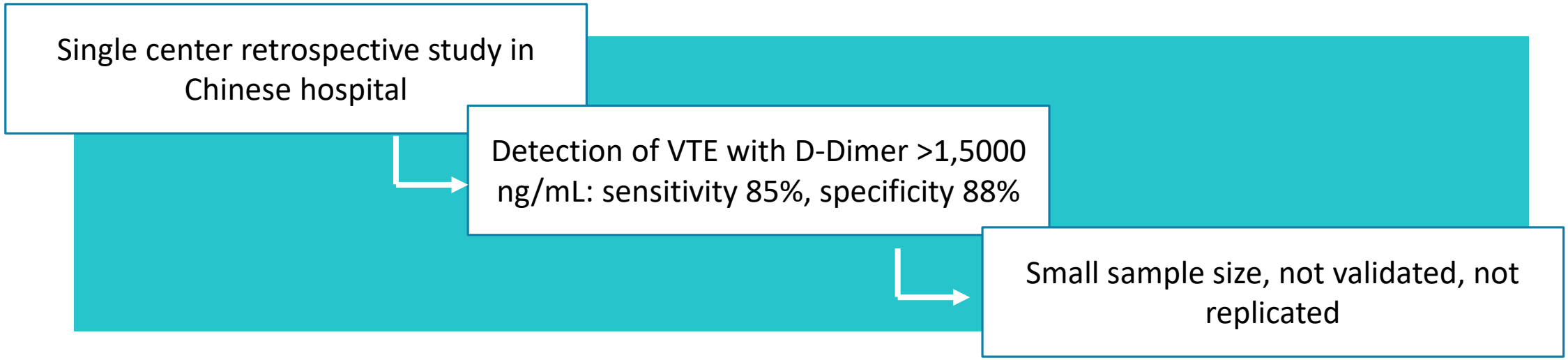
PT = prothrombin time; PTT = partial thromboplastin time; CRP = C-reactive protein; PLT = platelets

Typically less dramatic than in bacterial infections

Iba T. et al. *Crit Care Med* 2020; Volume online first issue: doi: 10.1097/CCM.0000000000004458.

Literature about how labs used

- Many studies assessing labs to predict risk of VTE development, mostly surrounding D-Dimer
- High D-dimers noted in severe COVID patients admitted to the ICU



Per the American College of Cardiology:
No great data to support diagnosis of VTE based off D-Dimer alone

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Guan W, et al. *N Engl J Med* 2020;382:1708-1720.
Huang C, et al. *Lancet* 2020;395:497-506.

Diagnosis

Practicality of diagnosis can be challenging

- Infection risk
- Patient instability

Ideally: **Imaging and Labs**

- D-Dimer not specific but can have a high negative predictive value
- CTPA
- VQ Scan
- ECHO assessing new right heart strain
- Ultrasound

Imaging not possible

Assess signs and symptoms:

- DVT manifestations
- Disproportionate hypoxemia
- New right ventricular dysfunction
- *Consider empiric treatment if high concern*

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.

Treatment

Professional Societies

- International Society on Thrombosis and Haemostasis (ITSH)
- American Society of Hematology (ASH)
- World Health Organization (WHO)
- American College of Cardiology (ACC)
- *Several more coming out!*

Thachil J, et al. *J Thromb Haemost* 2020;18:1023-1026.
Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973. (JACC)
COVID-19 and VTE/anticoagulation: FAQ. https://www.hematology.org/covid-19/covid-19-and-vte-anticoagulation. Accessed online 8/13/2020, last updated 7/20/2020.
World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected. Interim guidance 13 March 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf. Accessed 8/7/2020.

Professional Societies

Statements on VTE *Treatment* in COVID patients

ISTH	ASH	WHO	ACC
• No comment	• Consider drug-drug interactions with selection of agents • Prefer heparin or LMWH for hospitalized patients for shorter half life and less drug interactions • Consider underlying conditions, valves, etc	• No comment	• Enoxaparin may be favored if no contraindications acutely • Consider systemic fibrinolytics vs catheter-directed therapy in massive PE

Largely support pre-COVID VTE treatment guidance

Implications for Prevention and Treatment

Medication	Pros in COVID	Cons in COVID
UFH	• Potential role in decreasing disease progression • Short half-life • Minimal drug-drug interactions • Ability to monitor levels	• Higher need for monitoring and nursing contact time • Potentially longer duration to reach therapeutic targets
LMWH	• Potential role in decreasing disease progression • Minimal drug-drug interactions • Ability to monitor levels	• Renally cleared
Fondaparinux	• Once daily dosing to minimize nursing contact time	• Renally cleared
Warfarin	• Once daily dosing to minimize nursing contact time	• Drug-drug interactions with COVID therapies
DOACs	• 1-2 times daily dosing to minimize nursing contact time	• Drug-drug interactions with COVID therapies
tPA	• Postulated benefit during increased PAI-1 release (hypofibrinolytic state) during active COVID infection	• Really reserved for unstable PE • Not recommended as empiric therapy for microthrombi only

Useful drug-drug interaction resource: https://covid19-druginteractions.org/checker

Prophylaxis

Assessment of Severity

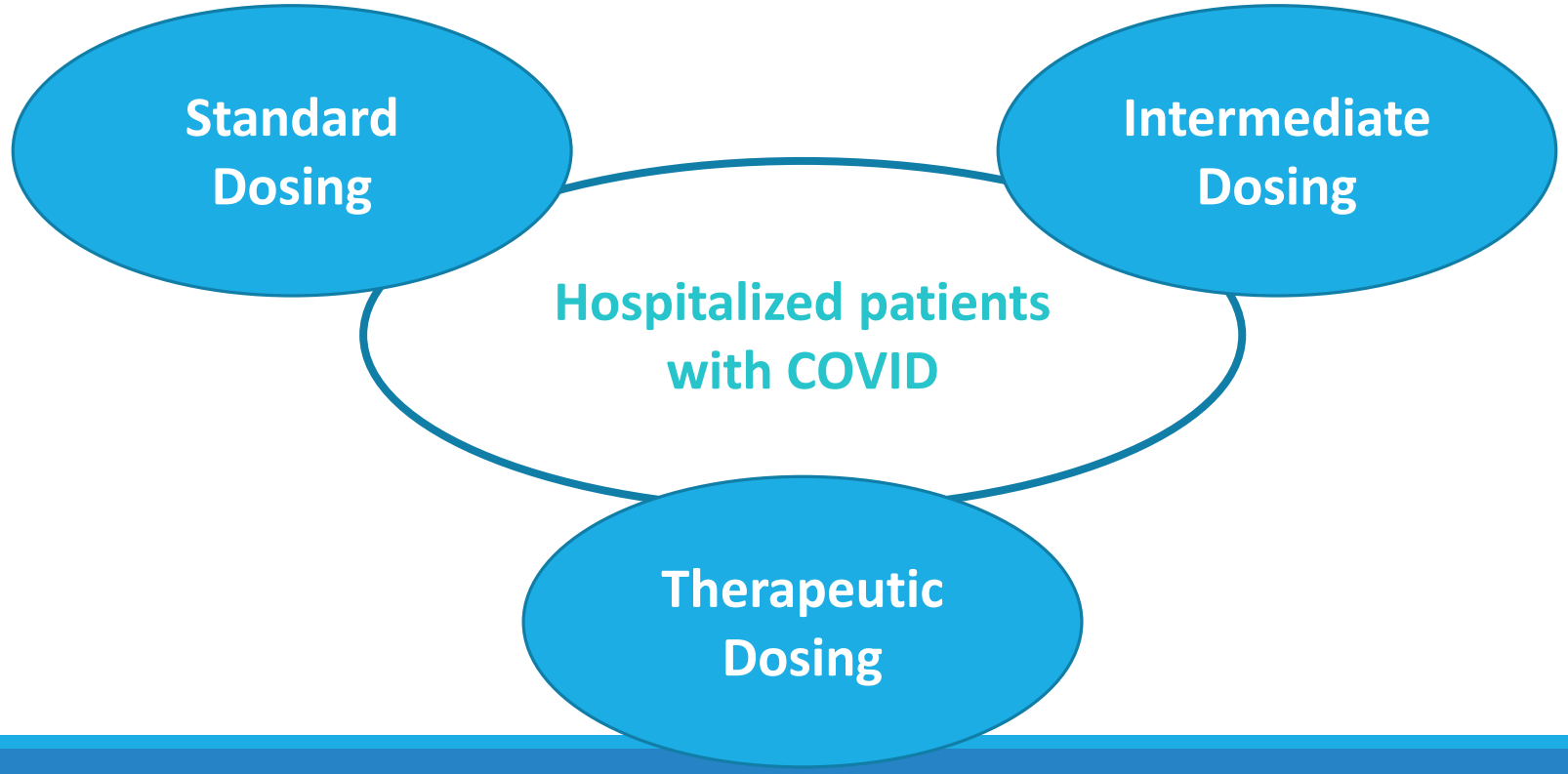
- Risks Assessment Methods to Consider:
  - PADUA scores in medically ill patients
  - Caprini scores in surgically ill patients
  - Sepsis-Induced Coagulopathy score
  - *No specific score validated in COVID patients*

This has led many institutions to develop individual risk assessments and approaches

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Iba T, et al. *BMJ Open* 2017;7:E017046.

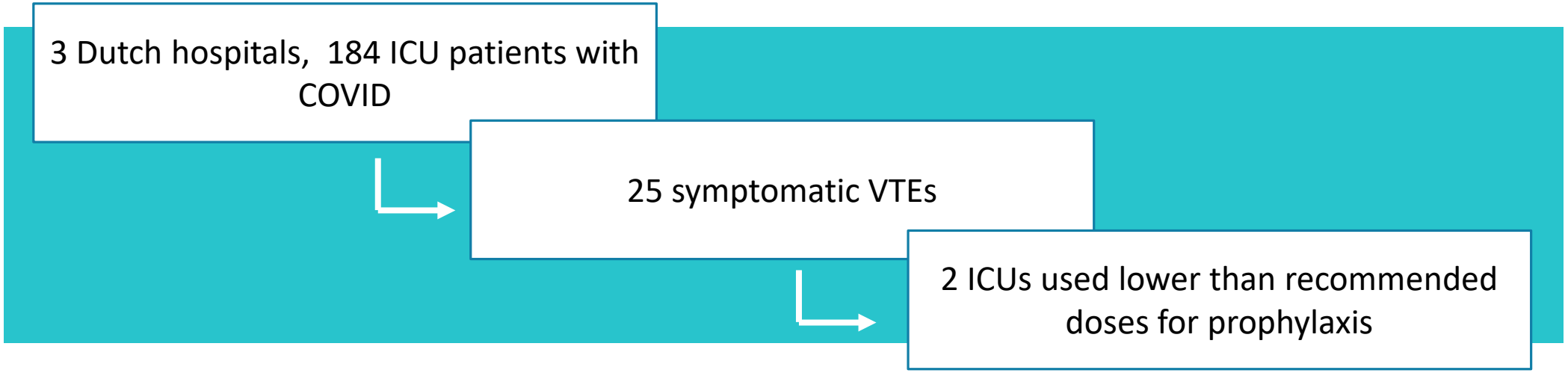
Approaches to therapy

Significant controversy surrounding dosage for VTE prophylaxis



Standard Dosing Approach

- COVID patients are typically adult, medically ill patients
- Initial and potential ongoing concern that this may not be enough



Unclear implications with inappropriate dosing

Klok K, et al. *Thromb Res* 2020;191:148-150.
Barnes GD, et al. *J Thromb Thrombolysis* 2020;50:72-81.

Intermediate Intensity Prophylaxis

- No specific studies available currently
- Several institutions have developed individualized approaches
  - Empiric twice daily dosing
  - Elevated Anti-Xa targets

- **Recommendations are currently just expert opinion**
- **Not yet well supported by the literature**

Bikdeli B. et al. *J Am Coll Cardiol* 2020;75(23)2950-2973.
Iba T, et al. *BMJ Open* 2017;7:E017046.

Empiric Full Dose Anticoagulation

- Several hospitals have published protocols incorporating empiric full dose anticoagulation

Single center retrospective observational study

Improved mortality and median survival days in mechanically ventilated patients with full anticoagulation vs not

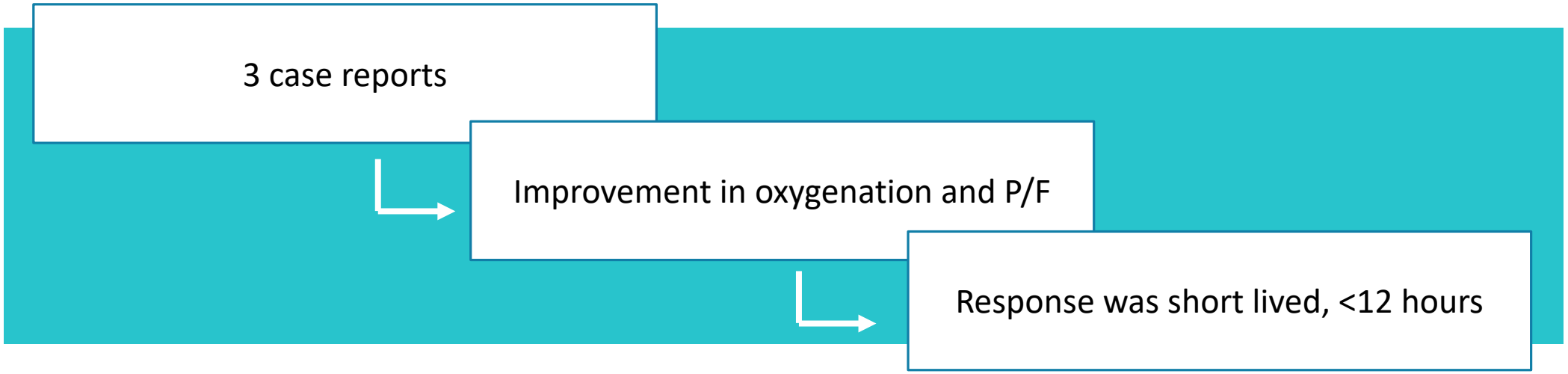
- No report of prophylactic dosing
- No account for baseline characteristics
- Did state if just prophylactic anticoagulation or none at all in the comparator group

Not well supported by the literature at this time

Paranjpe I, et al. *J Am Coll Cardiol* 2020;76:122-129.

Empiric tPA

- In the setting of presumed microthrombi in the lungs



Not well studied or justified currently

Wang J, et al. *J Thromb Haemost* 2020; doi: 10.1111/jth.14828.
Barnes GD, et al. *J Thromb Thrombolysis* 2020;50:72-81.

Professional Societies

Statements on VTE prophylaxis related to patients admitted with COVID-19

ISTH	ASH	WHO	ACC
• Prophylactic LMWH in all hospitalized patients with no contraindications	• Administer in all hospitalized patients • Favor LMWH over UFH to decrease contact time • Fondaparinux in HIT • Mechanical prophylaxis when chemical not available or contraindicated • Unknown if intermediate-intensity or full empiric anticoagulation beneficial • Unknown if post-discharge prophylaxis beneficial • No known benefit of empiric therapeutic anticoagulation in setting of elevated D-Dimer	• Preferred LMWH or heparin 5000 units SQ BID • Mechanical prophylaxis if contraindications	• Risk scores for VTE prophylaxis • Weight-based dosing needs to be further studied • Unknown benefit of empiric full anticoagulation • Pregnancy needs further studies for correct approach • Individual risk/benefit stratification for prophylactic post discharge anticoagulation ≤45 days

Largely support pre-COVID VTE prophylaxis guidance

Current Studies

Full Dose Vs Prophylactic Dose Heparin in High Risk COVID-19 Patients	
Design	Prospective, randomized active-comparator trial
Population	Adult high risk hospitalized patients with COVID diagnosis with O_2 requirement
Intervention	For VTE prophylaxis: • Therapeutic LMWH vs • Prophylactic or intermediate dose LMWH or UFH
Outcome	Composite: venous or arterial thrombotic events, all-cause mortality

Spyropoulos A, et al. June 9, 2020. Accessed August 19, 2020. https://clinicaltrials.gov/ct2/show/NCT04401293

Question 2

69 year old female presents to your ED with cough, shortness of breath, and positive COVID nasal swab 4 days prior to arrival. She is requiring high flow nasal cannula 70 L 100% with oxygen saturations ~85%. The team decides to intubate and she is admitted to the medical ICU. They are working to enroll her in clinical trials for COVID therapies. Patient reports no current home medications, but had recently moved here from Argentina. She is found to have an A1c of 14% on arrival. Some presenting data are as follows: WBC 13, D-dimer 115, CrCl ~75 mL/min (making appropriate urine), BMI 45 kg/m^2.

What do you recommend for DVT prophylaxis in this patient?

A. Enoxaparin 40 mg SQ daily
B. Enoxaparin 40 mg SQ BID
C. Heparin 80 units/kg bolus, followed by 18 units/kg/hr
D. Warfarin 5 mg day

Take Home Points

- COVID patients, particularly critically ill tend to be at high risk for development of VTE
- Unknown significance of D-dimer, except that *potentially* high risk for clot, and still carries good negative predictive value
- VTE diagnosis in COVID patients can be challenging
- Treatment is per usual, but mindful of drug-drug interactions and nurse contact time
- Prophylaxis definitive statements are still challenging and more data is needed

Coagulopathies in COVID

IMPLICATIONS FOR VTE PROPHYLAXIS AND TREATMENT

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September 12, 2020
USHP Winter Meeting