

Pharmaceutical Supply Chain Management before, during and after the inpatient CoVID 19 pandemic surge(s)

John Hrenko, Gordon Hubbard, Jaime Levash, Margaret Stephan, Ifeoma Eche, Howard Seth Gold, Julius Yang, Christopher McCoy.
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Introduction/Problem

In February of 2020, our group purchasing organization announced concerns for supply chain disruptions given the reliance on active pharmaceutical ingredient (API) production from China. Conversely, none of the wholesale distributors were experiencing any supply disruptions and that they anticipated none. Historic experience with high acuity influenza surges (2009, 2017) and natural disasters (Hurricane Maria) lent perspective to the potential impact of manufacturing and disproportionate demand leading to shortages. However, the trajectory of this yet to be defined global pandemic left Pharmacy Operations and Clinical Management without a clear direction for anticipatory purchasing or a watch and wait approach. After weeks, medications of concern affected were agents thought to treat CoVID-19 (e.g. hydroxychloroquine, azithromycin), and agents to treat the symptoms of CoVID-19 (e.g. respiratory medications-inhalers, nebulizers). As the pandemic intensified, agents to address the influx of intensive care admissions (e.g., vasopressors, sedatives, intravenous opioids, neuromuscular blockers) became on short supply. The shortage list continued to expand faster than any other time period across multiple categories threatening to interrupt patient care.

Aim/Goal

To balance unclear and fast evolving demand with supply chain availability, fiscal responsibility, clinical evidence, and avoiding a hoarding process, to avoid negative consequences in patients. There are no available benchmarks for shortages other than avoiding stockouts, implementing therapeutic substitutions and forestalling negative clinical outcomes.

The Team

- | | | |
|-----------------------------|------------------------|--|
| ➤ John Hrenko, PharmD | Operations Supervisor | Department of Pharmacy |
| ➤ Gordon Hubbard | Purchasing Manager | Department of Pharmacy |
| ➤ Jamie Levash RN | Project Manager | Health Care Quality |
| ➤ Margaret Stephan MS | Chief Pharmacy Officer | Department of Pharmacy |
| ➤ Ifeoma Eche, PharmD | Clinical Manager | Department of Pharmacy |
| ➤ Howard Seth Gold, MD | Clinical Director | Health Care Quality, Infectious Diseases |
| ➤ Julius Yang, MD | Clinical Director | Health Care Quality |
| ➤ Christopher McCoy, PharmD | Clinical Manager | Department of Pharmacy |

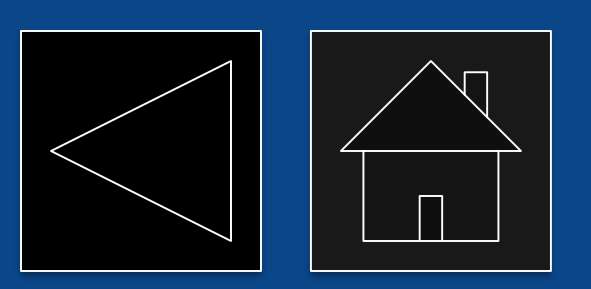
The Interventions

- Given the escalation and dynamic nature of supply chain disruptions daily huddles and communications were enlisted,
- Purchasing and Pharmacy Operations Administration continuously monitored supply chain announcements from multiple sources, the group purchasing organization, manufacturers, wholesalers multiple times a day.
- Purchasing sought out alternate suppliers and allocation methods to order/purchase items in high demand continuously.
- Pharmacy Operations used tactics including centralization of product supply, alternative route selection.
- Clinical Pharmacy Managers worked with Infectious Diseases/Antimicrobial Stewardship to investigate and reported out guidance relative to CoVID 19 therapeutics (e.g. high demand for azithromycin and hydroxychloroquine). Alternate dosing strategies and algorithms for pain management, sedation and neuromuscular blockade were created to standardize practice.
- Invocation of the Drug Shortage Task Force including Health Care Quality was used to prioritize care, build consensus with thought leaders and experts and devise algorithms and protocols.
- A continuous modification of Provider Order Entry clinical decision support was designed and implemented to guide best care and avoid shortages

Detailed interventions

- Identify the key medications to treat the complications of CoVID 19 infection.
- Dyspnea/Pneumonia
 - Inhalers/nebs
 - Antitussives
 - Expectorants
 - Sepsis
 - Vasopressors
 - Sedatives
 - Antibiotics
 - Analgesics
 - Supportive meds
 - Neuromuscular Blockers
 - Experimental CoVID tx
 - Antibiotics
 - Antivirals

Drugs completely out at the manufacturer and wholesaler level		
Respiratory	Intensive Care Unit Supportive	CoVID experimental therapeutics
Albuterol Inhaler	Artificial Tears	Azithromycin IV
Albuterol Neb	Chlorhexidine Gluconate PO	Azithromycin PO
Budesonide NEB	Sodium Bicarbonate IV	Chloroquine PO
Epoprostenol IV		Cobicistat PO
Ipratropium Bromide Inhaler	Sedatives	Darunavir PO
Ipratropium Bromide Neb	Dexmedetomidine IV	Doxycycline PO
Tiotropium inhaler	Ketamine IV	Doxycycline IV
	Midazolam IV	Hydroxychloroquine PO
Electrolytes	Propofol IV	Lopinavir-Ritonavir PO
Calcium Gluconate IV		
Magnesium Sulfate IV	Antibiotics	Neuromuscular Blockers
	CefePIME IV	Cisatracurium Besylate IV
Vasopressors	CefTAZidime IV	Etomidate IV
EPINEPHrine IV	CefTRIAxone IV	Rocuronium IV
NOREpinephrine IV	Piperacillin-Tazobactam IV	
Phenylephrine IV	Vancomycin IV	Symptom Care
Vasopressin IV		Benzonatate PO
	Analgesics	GuaiFENesin PO
	Fentanyl IV	GuaiFENesin-Dextromethorphan PO
	HYDROmorphone IV	Ondansetron IV



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More Results/Progress to Date

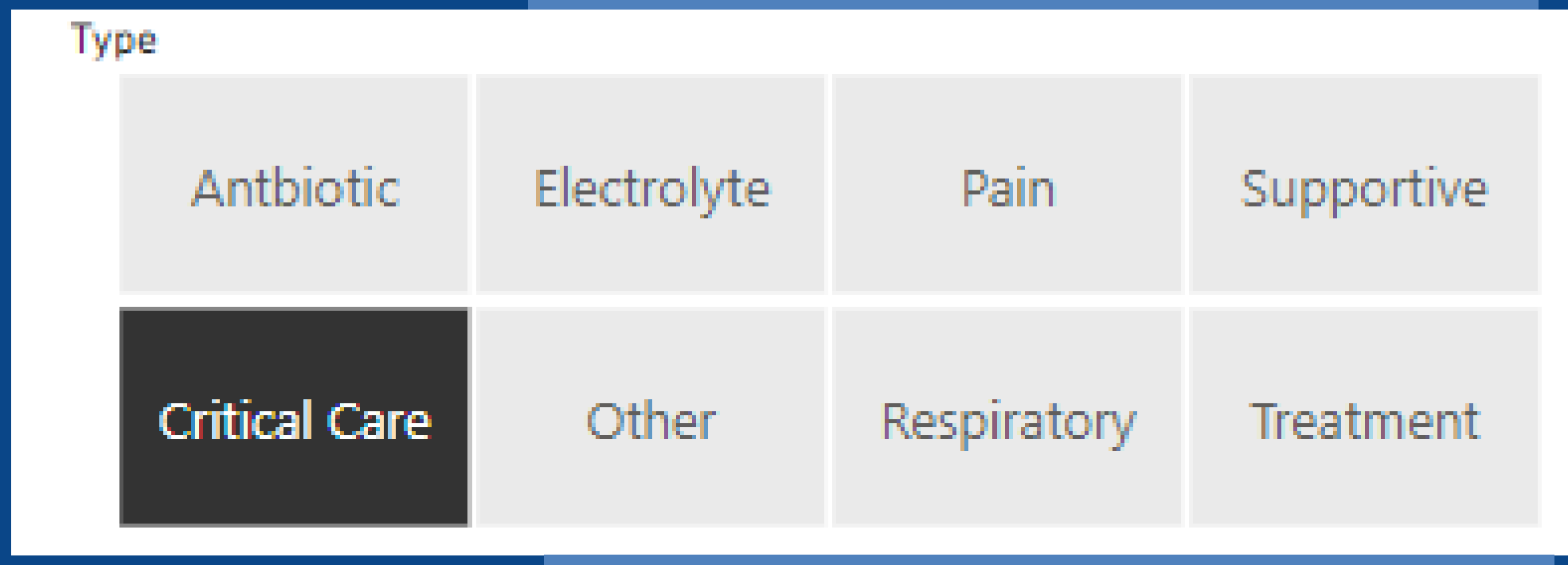
BIDMC Pharmacy Planning Matrix COVID-19

- Watchful attention to API and medications from China and India and other affected areas
- Monitor Health Trust, ASHP, wholesalers, etc.
- Stockpiling is not recommended at this time
- Current recommendations:
 - Maintain medications focused on supportive care – consider increasing supplies of vancomycin, 3rd/4th generation cephalosporins, and pressors for potential surge units
 - Maintain/increase supplies of cleanroom garb (masks, gowns, gloves, alcohol-based cleaning and hand-washing supplies)
 - Increasing par levels of antiviral therapies not recommended at this time
 - Maintain medications to support chronic conditions due to increased hospitalizations (diabetes, CHF, COPD, etc.)
- Leading investigational therapy remdesivir (Gilead®) used in Washington state but no compassionate use protocol available
- Other leading therapies include Kaletra and interferon (both commercially available)
 - None of the therapies are recommended by CDC or WHO for use in the US

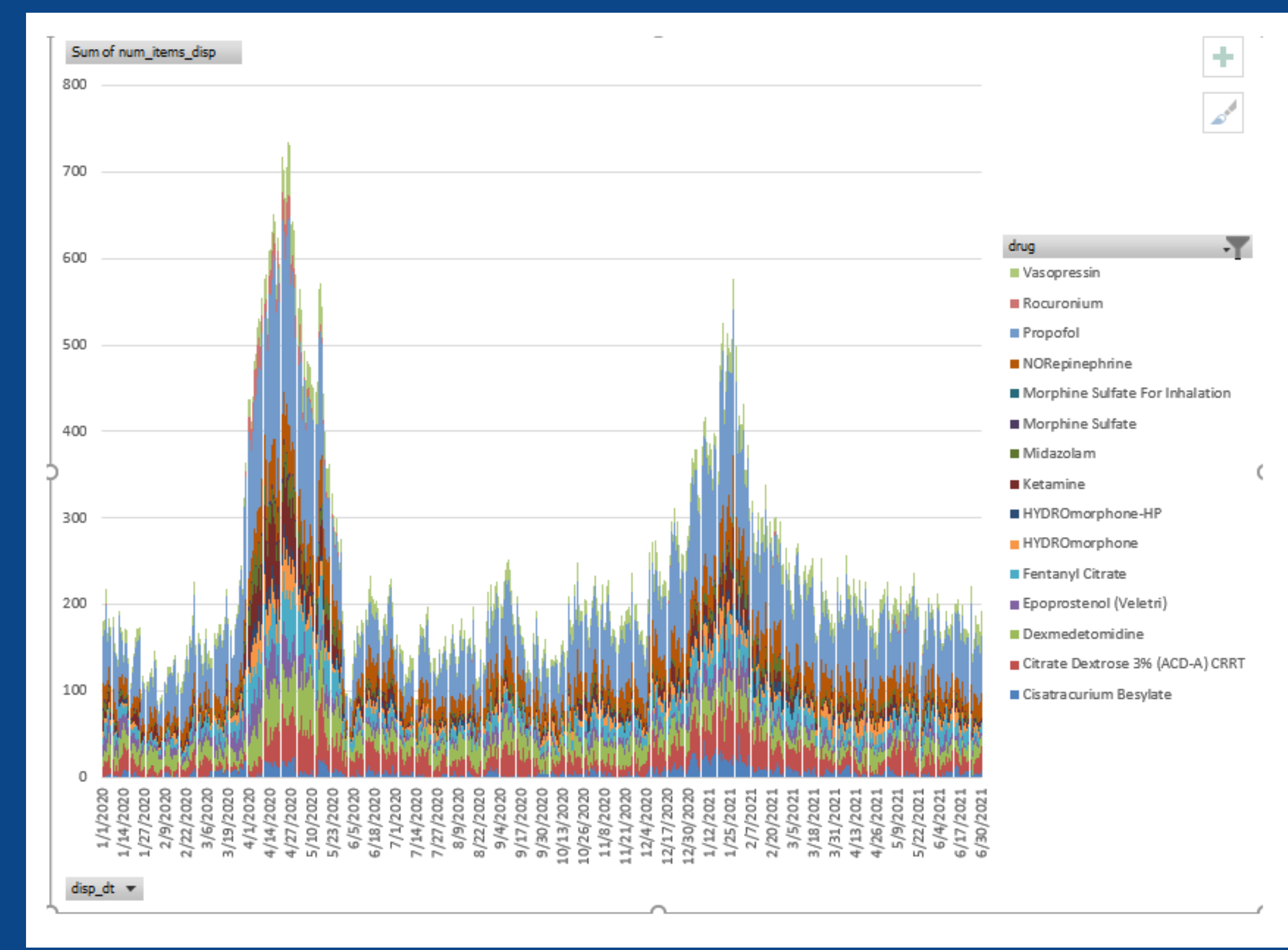
Pharmacy COVID-19 Key Members:

- John Hrenko – Emergency Management and Drug Utilization
- Chris McCoy – ID
- Shawn Wood, Gordon Hubbard, Yu Choi – Pharmacy Supply Chain
- Tom Slepka, Peggy Stephan

Therapeutic specific demand and utilization during surge 1 & 2.

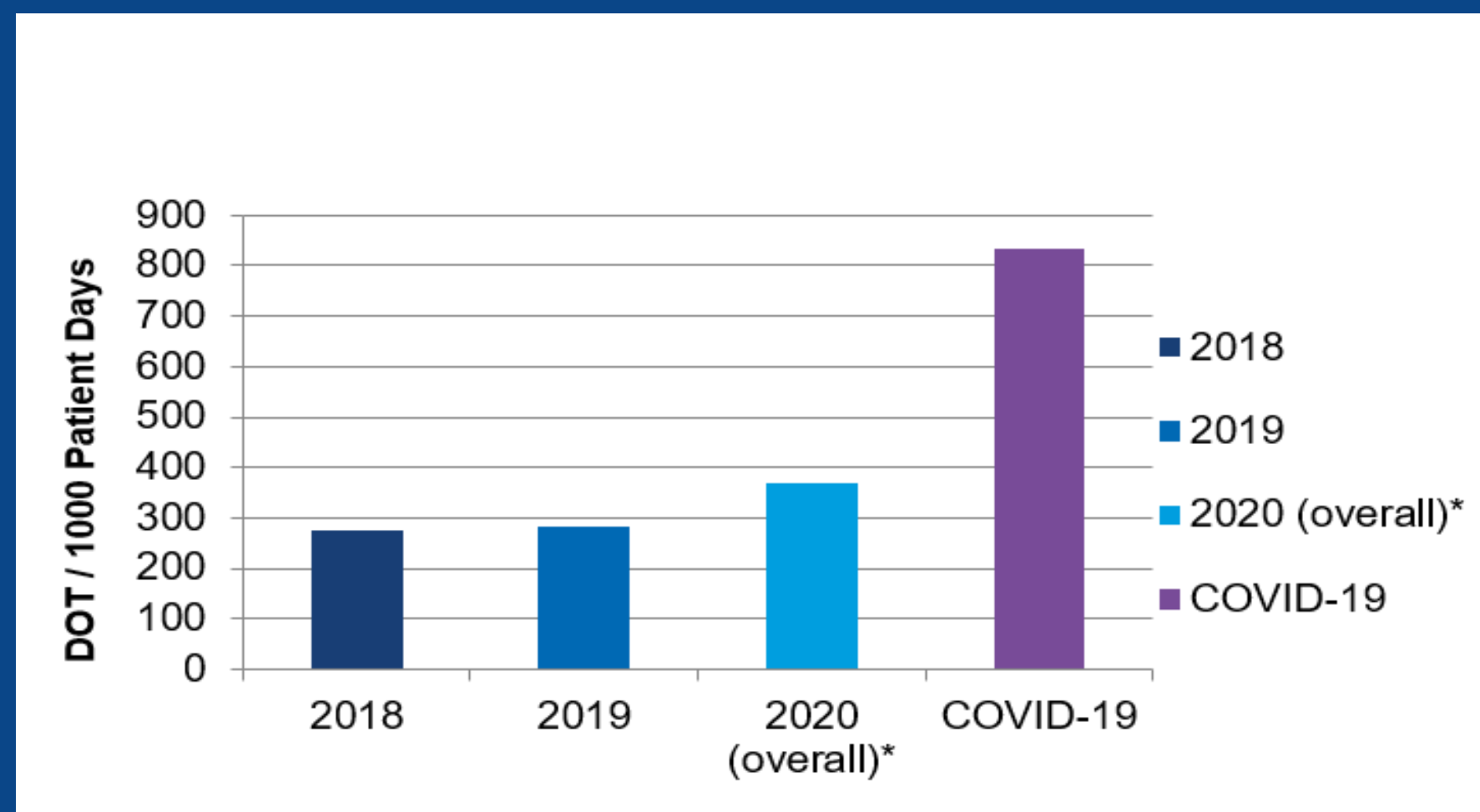


Introduction of a Performance Manager View



Overarching Planning and Execution detailed for our team

Continuous monitoring of demand and retrospective lookbacks:



Antibiotic demand during the first surge of 3 months dwarfed antibiotic use for years prior and patients with CoVID were 10x more likely to receive antibiotics. Continuous shifts directed by our team were necessary to keep supply.

Rx_disp	Item_id	Par Level in main Rx	AMU	TARGET SAFETY STOCK	Average Daily Use	Normal Stock (OOH)	Supply in omnicells	CURRENT SAFETY STOCK	TOTAL STOCK	Current days of Safety stock	Day on hand TOTAL STOCK	% to Goal
Albuterol Inhaler	PROAIRB.5H	46	138	414	4.6	112.0	45.0	157.0	0.0	34.1	0%	
Albuterol Inhaler	ALBU17H	80	240	720	8.0	11.0	88.0	429	528.0	53.6	66.0	
Albuterol 0.083% Neb Soln 1Neb	ALBU3H	570	1710	5,130	57.0	502.0	1267.0	4320	6089.0	75.8	106.8	
Artificial Tears GEL 1% DRP	THER10	300	700	1,400	23.3	180.0	393.0	900	1473.0	38.6	63.1	
Artificial Tears Preserv 0.4 mL EACH (UD)	REFRESH	360	1080	2,160	36.0	246.0	549.0	1900	2695.0	52.8	74.9	
Azithromycin 500 mg vial	AZITS001	80	240	480	8.0	6.0	23.0	150	179.0	18.8	22.4	
Azithromycin 250 mg tablet	ZITHR250	350	1050	2,100	35.0	1381.0	552.0	1908	3841.0	54.5	109.7	
Benzonatate 100mg CAP	BENZ100	500	1500	3,000	50.0	329.0	418.0	1500	2247.0	30.0	44.9	
Budesonide Neb 0.5mg/2mL 2mL NEB	BUDE0.5	165	495	990	16.5	87.0	15.0	690	792.0	41.8	48.0	
Budesonide Neb 0.25mg/2mL 2mL NEB	BUDE0.25	90	270	540	9.0	94.0	#N/A	420	#N/A	46.7	#N/A	
Calcium Gluconate (Premix) 2g/100mL 100mL B	CALCG2/100NACL	216	648	648	21.6	252.0	155.0	407.0	407.0	0.0	18.8	
CefePIME 1g VIAL	CEFE11	500	1500	3,000	50.0	206.0	201.0	1010	1417.0	20.2	28.3	
CefePIME 2g VIAL	CEFE21	1800	5400	10,800	180.0	799.0	462.0	4020	5281.0	22.3	29.3	
CeftAZidime 1g VIAL	CEFT1V	550	1650	3,300	55.0	274.0	157.0	850	1281.0	15.5	23.3	
CeftAZidime 2g VIAL	CEFT21	250	750	1,500	25.0	177.0	242.0	780	1199.0	31.2	48.0	
CeftTRIAxone 2gm VIAL	CEFR21	250	750	1,500	25.0	136.0	237.0	700	1073.0	28.0	42.9	
CeftTRIAxone 1gm VIAL	CEFR11	425	1275	2,550	42.5	292.0	359.0	1195	1846.0	28.1	43.4	
Chlorhexidine Gluconate 15 mL UDCUP	CHLO15L	520	1560	3,120	52.0	476.0	452.0	1700	2628.0	32.7	50.5	
Chloroquine 250mg TAB	CHLOR250	90	270	540	9.0	88.0	#N/A	200	#N/A	22.2	#N/A	
Cisatracurium Besylate 20 mg/10 mL VIAL	CISA201	37	22	44	0.7	49.0	36.0	114	199.0	155.5	271.4	
Cisatracurium Besylate 200mg/20mL 20mL VIAL	CISA2001	0	53	159	1.8	0.0	#N/A	100	#N/A	56.6	#N/A	
Cobicistat 150mg	COBI150	55	165	165	5.5	84.0	#N/A	120	#N/A	21.8	#N/A	
Darunavir 800mg	DARU800	70	210	210	7.0	104.0	43.0	210	357.0	30.0	51.0	
Dexmedetomidine 0.2mg/2mL 2mL VIAL	DEXM2001	700	2100	6,300	70.0	523.0	305.0	1050	1878.0	15.0	26.8	
Doxycycline 50 mg capsule	DOXY50	135	405	810	13.5	31.0	71.0	700	802.0	51.9	59.4	
Doxycycline 100 mg capsule	DOXY100C	270	810	1,620	27.0	182.0	564.0	1250	1996.0	46.3	73.9	
Doxycycline 100 mg vial	DOXY1001	40	120	240	4.0	12.0	28.0	290	330.0	72.5	82.5	
EPINEPhrine 1 mg/1 mL AMP	EPI11	530	1590	3,180	53.0	506.0	590.0	1010	2106.0	19.1	39.7	
Epoprostenol 1.5mg vial	VELE1.51	145	435	870	14.5	234.0	#N/A	#N/A	#N/A	0.0	#N/A	
Epoprostenol 0.5mg vial	VELE0.51	75	225	450	7.5	95.0	#N/A	#N/A	#N/A	0.0	#N/A	
Etomidate 20mg/10mL 10mL VIAL	ETOM21	85	255	510	8.5	86.0	293.0	200	579.0	23.5	68.1	
Fentanyl 2.5mg 50mL Bag	FENT2.550	160	480	960	16.0	172.0	42.0	214.0	214.0	0.0	13.4	

Tracking and movement of key meds with grading of next phase readiness.

- Par levels needed to be adjusted to the new normal for daily/monthly utilization
- A safety stock to get through national shortages was required but had to balance fiscal responsibility and good global citizenship (e.g. no hoarding)
- Omicell (floor supply) had to be readjusted to meet new floor demands and centralization.

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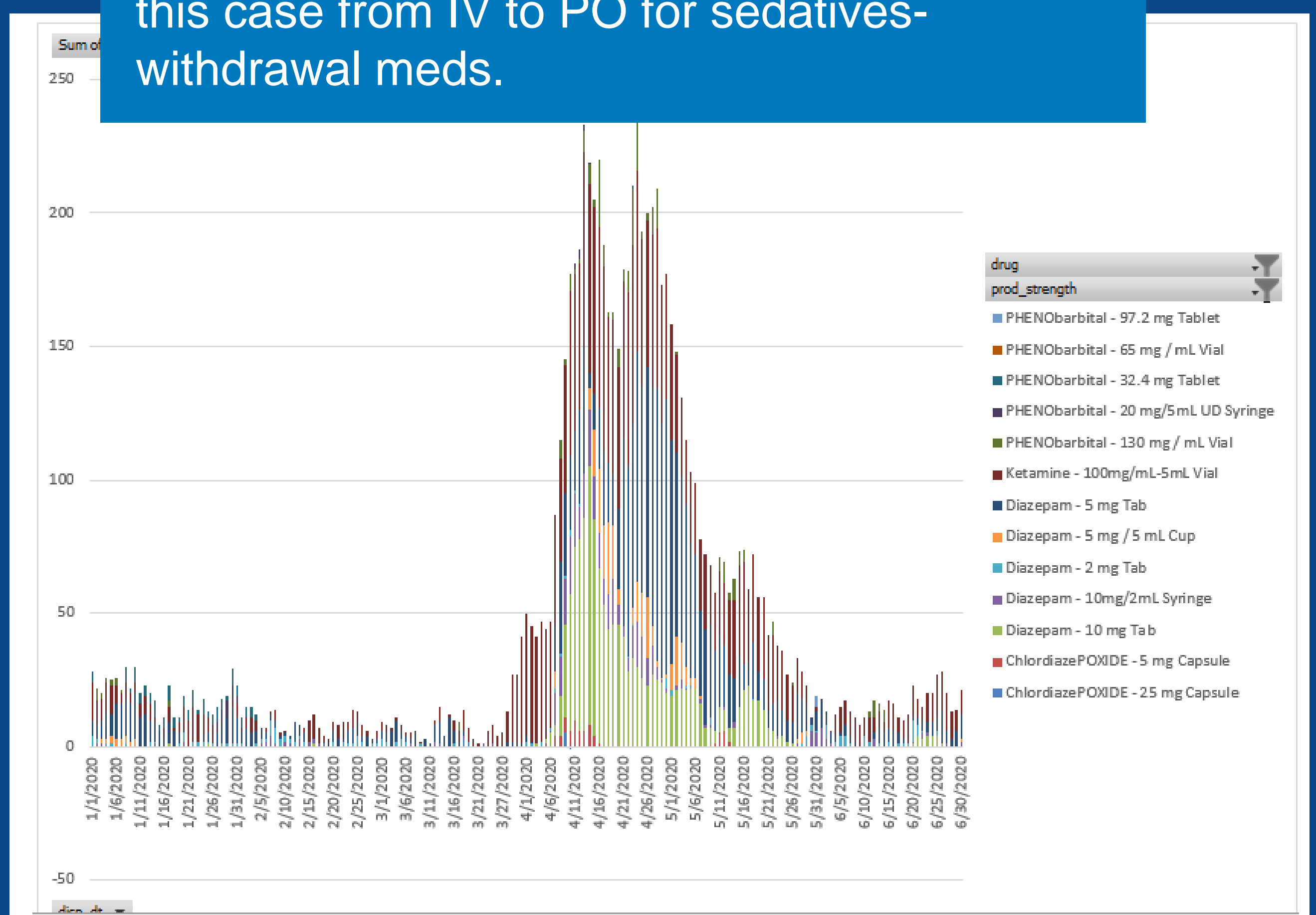
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More Results/Progress to Date

Situational awareness and community building

- Standard processes for ordering preparing and administering meds all required reframing across disciplines

Example of adjustment to steep demand curves through therapeutic substitutions, in this case from IV to PO for sedatives-withdrawal meds.



Example communications to all Hospital Staff

In order to rein in the reflexive use of agents thought to aid in treatment of the infection given short supply and prophylactic use.

Subject: Agents for potential treatment of COVID-19


Like many institutions, BIDMC is experiencing a shortage of medications used in the treatment of COVID-19 in hospitalized patients. As we do not know the trajectory of need over the next few weeks to months, we do know that demand will outstrip supply. Institutional guidelines are forthcoming. Medications that are included in the guideline include:

- Hydroxychloroquine Sulfate 200 mg TAB
- Lopinavir-Ritonavir 200mg/50mg 1TAB TAB
- Lopinavir-Ritonavir solution
- Darunavir 800 mg
- Cobicistat 150 mg
- Chloroquine 250/500mg TAB
- Tocilizumab IV

What You Need to Know:

1. **It is imperative that we conserve our existing supply of these agents for treatment of COVID-19**
2. Prescribers should **avoid use of any of these agents for prophylaxis**
3. In the case of Hydroxychloroquine, prescribers may consider a patient's own supply or holding the medication temporarily if not a medical necessity
4. In the case of Lopinavir/ritonavir and Darunavir/cobicistat for HIV/AIDS, given that these are infrequently used for this indication, prescribers may consider a patient's own supply or holding the medication temporarily if not a medical necessity

Practice Alert
Return of Intubation Medication Kits to Pharmacy


 Beth Israel Deaconess Medical Center

What is new? Early pandemic guidance suggested that all items be disinfected to protect staff


For an emergent intubation, intubation medication kits can either be retrieved from the Omnicell (patient care areas listed below), or from a Pharmacist responding to a Code Blue event. During this COVID-19 pandemic, Pharmacy needs to ensure any returned kit is disinfected.

The intubation medication kit contains the following:

Etomidate 2 mg/mL, 10 mL vial	Lidocaine 100mg Bristojet syringe
Oxymetazoline HCl 0.05% spray	Rocuronium 10mg/mL, 10mL vial
Phenylephrine 1mg/10mL syringe	Propofol 10mg/mL, 20 mL vial
Succinylcholine 20 mg/mL, 5 mL syringe	Lidocaine 2% Jelly, 5mL tube



Practice Alert
Albuterol MDI Conservation

 Beth Israel Deaconess Medical Center

What is New? Nebulizer treatments are considered high risk, aerosol-generating procedures requiring increased PPE requirements and resource utilization to mitigate the potential spread of COVID-19 to the healthcare professional administering the treatment. For this reason, if there is a clinical indication for albuterol as a bronchodilator, MDI formulation should be reserved for COVID-19 rule-out/positive patients.

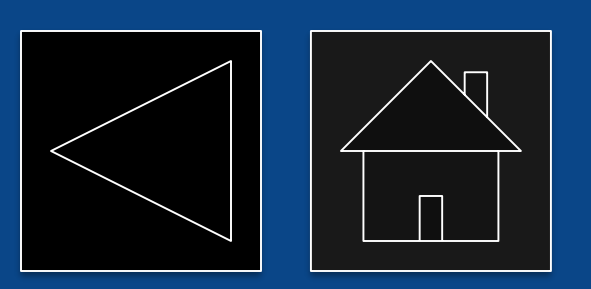
As a result, we are monitoring stock of albuterol MDIs and the need to conserve use due to high risk patients undergoing COVID-19 evaluation and those who are COVID-19 positive.

How can you help? When processing orders for new albuterol MDI and/or responding to an "RN Request" for a new or missing albuterol MDI we must determine if the MDI is necessary or if the patient can be treated with albuterol nebulizer treatments.

New Albuterol MDI orders:

- PRN orders – do not send inhaler upon order verification, wait for RN to request
- Review selected indication to ensure for "possible/confirmed COVID-19 patient"

Inhalers became in such short supply but critical to care of all inpatients



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More Results/Progress to Date

Drug substitutions were necessary but required education and communication.

Example communications and clinical therapeutic summaries

How can you help?

At this point, please **reserve cisatracurium** for patients with advanced renal OR advanced hepatic failure, and use **rocuronium** as the first line neuromuscular blockade agent in the ICU. Our goal is to continue to balance the use of both agents to avoid a shortage of rocuronium. There is now a prompt in POE that guides clinicians to order rocuronium when they attempt to order cisatracurium.

Standard dosing and titration instructions are available in cPOE and in the Critical Care Titration Guidelines on the PPGD. The IV guidelines and sigma pumps are also up to date.

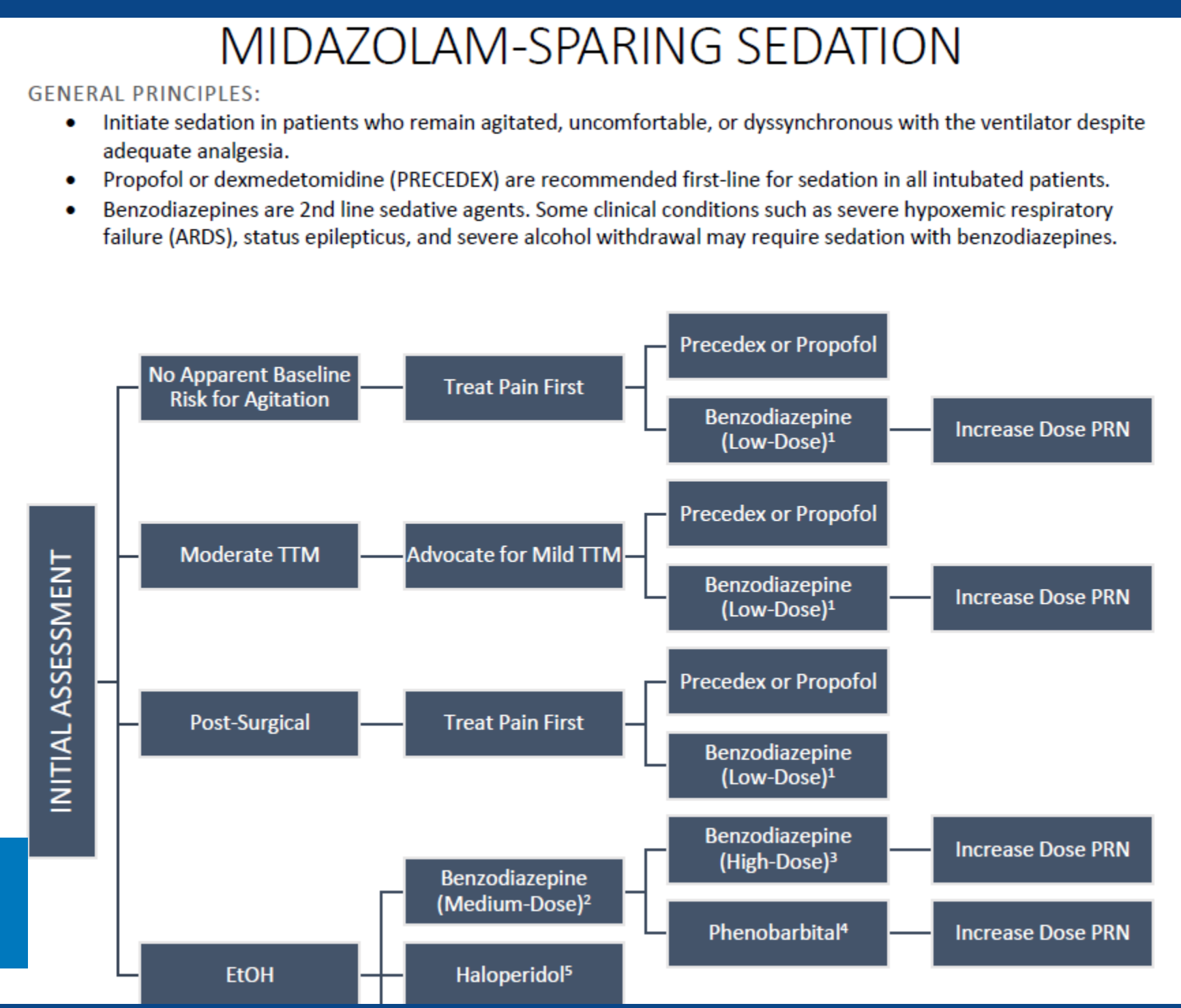
Key clinical differences between agents are summarized in the table below:

	Cisatracurium	Rocuronium
Half-Life	25 minutes	60 minutes
Duration	Recovery in 30 minutes	Recovery in ~ 30 minutes. May be prolonged in advanced renal or advanced hepatic failure
Excretion	Hoffman elimination	50% feces/30% urine
Dose adjustment in organ failure	No	Renal failure – no Hepatic failure – may require dose reduction
Loading Dose	20mg (or 0.2 mg/kg)	50 mg (or 0.6 mg/kg)
Maintenance dose (infusion)	0.15-0.5 mg/kg/hr	8-16 mcg/kg/min

Cisatracurium outages

Midazolam critical lows

Fentanyl Mitigation



Drug Shortage Task Force Prioritization Schemes

Table 3. Assigning Patients to Color-coded Priority Groups

Use Raw Score from Multi-principle Scoring System to Assign Priority Category

Level of Priority and Code Color	Priority score from Multi-principle Scoring System
RED Highest priority	Priority score 1-3
ORANGE Intermediate priority (reassess as needed)	Priority score 4-5
YELLOW Lowest priority (reassess as needed)	Priority score 6-8

Lessons Learned

- Therapeutic demand and supply chain interruption is nearly impossible to predict during a global pandemic
- Interdisciplinary involvement and broad communications are essential to keep available supply and ensure public health safety
- Time required to address all the clinical decision making, inventory control and supply allocation is more than 50% of dedicated time.

Next Steps

- Utilize similar tactics for management of acute shortages early with engagement of therapeutic area leads, inventory tracking and demand curves.
- Apply modeling for network engagement and resource sharing.
- Utilize global facing platforms like PowerBI through Performance Manager.

