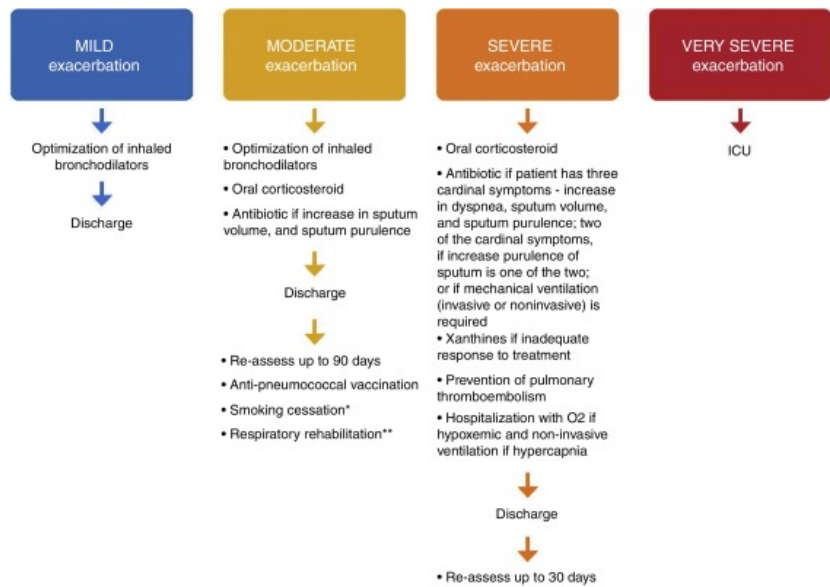
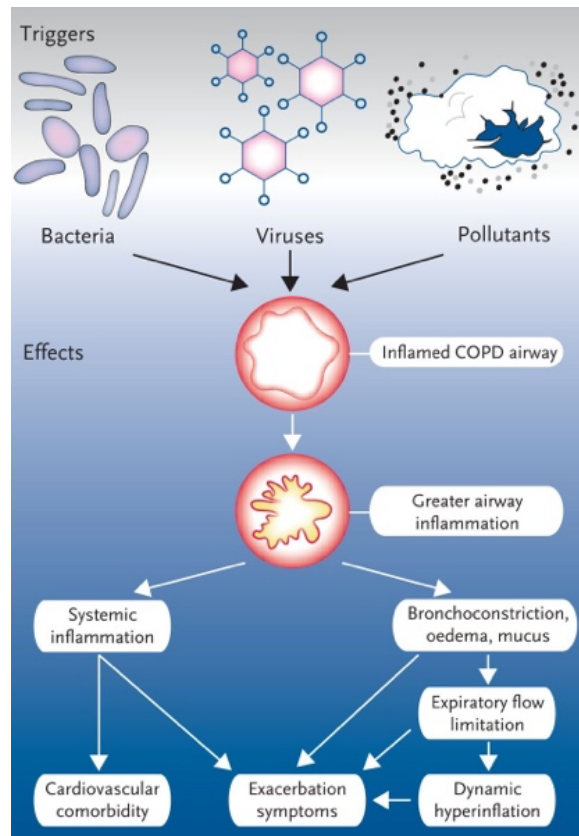


COPD Exacerbation

- The “Global Initiative for Chronic Obstructive Lung Disease (GOLD)” defines COPD exacerbation as “an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”



- Antiviral Agents:** The majority of COPD exacerbations are triggered by respiratory viral infections. Bacterial pathogens are secondary invaders after a viral trigger.
 - If COPD exacerbation is triggered by an influenza virus, oseltamivir (Tamiflu) is recommended.
 - Oseltamivir 75 mg PO BID x 5 days (CrCl \geq 60 ml/min)
 - Oseltamivir 30 mg PO BID x 5 days (CrCl 31-59 ml/min)
 - Oseltamivir 30 mg PO daily x 5 days (CrCl 10-30 ml/min)
 - If COPD exacerbation is triggered by Covid-19, Paxlovid (nirmatrelvir 150 mg / ritonavir 100 mg) PO BID x 5 days is recommended over Lagevrio (molnupiravir) 800 mg PO BID x 5 days.
 - Nirmatrelvir 300 mg / Ritonavir 100 mg PO BID x 5 days (eGFR \geq 60 ml/min)
 - Nirmatrelvir 150 mg / Ritonavir 100 mg PO BID x 5 days (eGFR 30-59 ml/min)
 - If eGFR < 30 ml/min, consider molnupiravir 800 mg PO BID x 5 days, since molnupiravir is eliminated by the liver.



- Moderate-severe COPD exacerbation is identified in patients who present with 2 of the 3 following symptoms OR in patients who require hospitalization.

(1) increased dyspnea (2) increased sputum volume (3) increased sputum purulence

- Antibiotics** are prescribed in COPD exacerbation if increased dyspnea is accompanied with increased sputum volume or increased sputum purulence. Antibiotics are also prescribed in patients who require hospitalization.

- **Bronchodilators:** All patients with COPD exacerbation should receive treatment with a SABA since albuterol and levalbuterol (Xopenex) have a rapid onset of action and high efficacy.



- SABA-SAMA (albuterol 2.5 mg / ipratropium 0.5 mg) combination therapy is superior to albuterol alone in stable COPD, but studies in acute exacerbations are limited; however most clinicians prefer using SABA-SAMA combination therapy rather than SABA alone in patients with COPD exacerbation.



- Levalbuterol (Xopenex) dosing for nebulization is 0.63 - 1.25 mg and is administered at the same interval as albuterol.
- Side effects of SABA include hypokalemia, tachycardia, cardiac arrhythmias. Levalbuterol minimizes cardiac adverse effects.

- **Magnesium sulfate** 2 gm IVPB over 20 minutes in severe exacerbation that is not responding to short-acting bronchodilators.

- MOA: Magnesium inhibits calcium influx into airway smooth muscle cells.
- Magnesium sulfate is contraindicated in renal failure; hypermagnesemia may result in muscle weakness.



- **Glucocorticoids:** Short courses of oral or intravenous glucocorticoids are recommended in moderate to severe COPD exacerbation for inpatient and outpatient use.

- Prednisone 40-60 mg PO daily x 5-14 days
- Methylprednisolone (Solu-Medrol) 60 mg IV daily to Q6H, depending on severity.



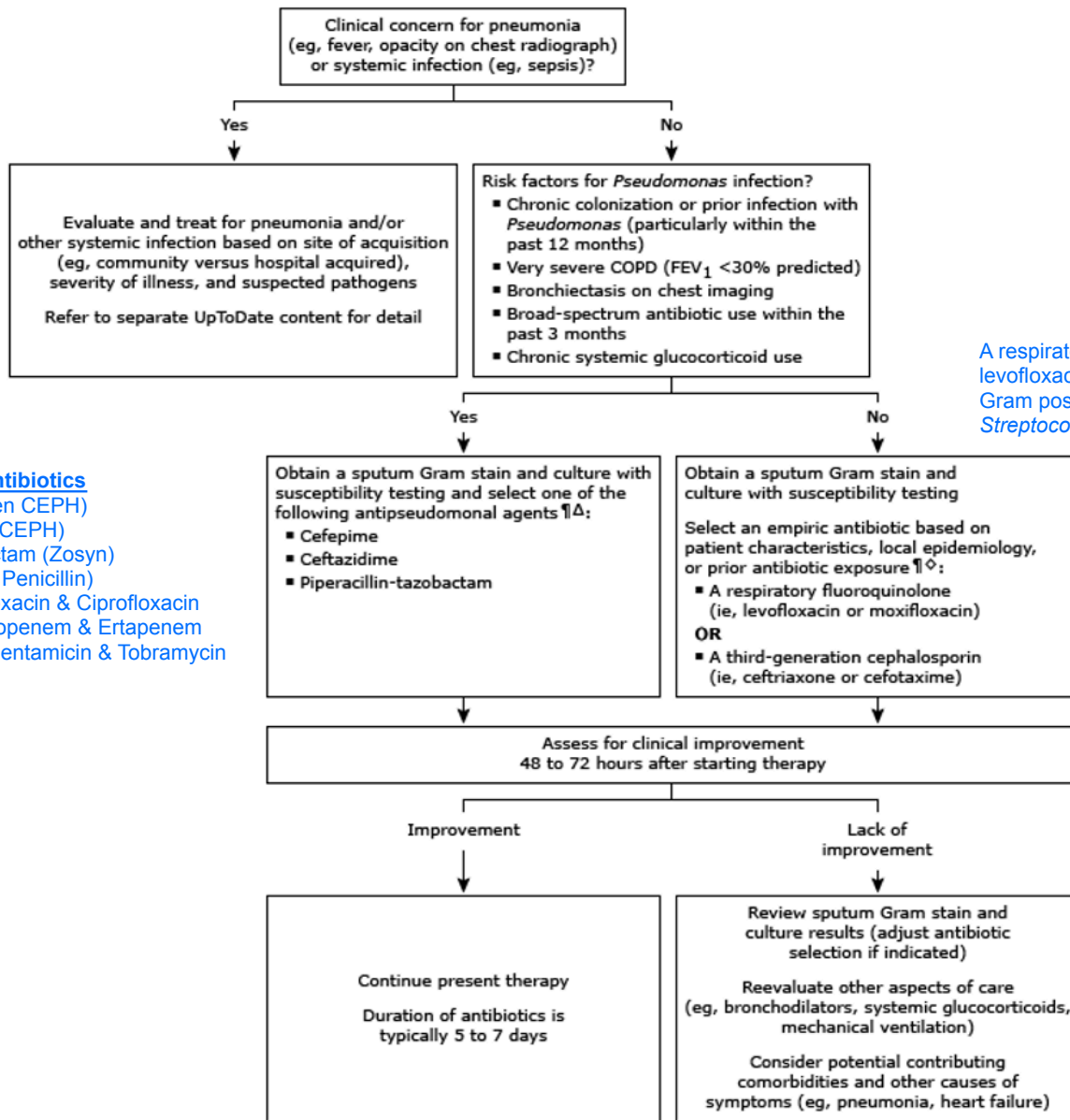
Comparison of Systemic Glucocorticoid Preparations (UpToDate)

	Equivalent doses (mg)	Antiinflammatory activity relative to hydrocortisone*	Duration of action (hours)
Glucocorticoids			
Short acting			
Hydrocortisone (cortisol)	20	1	8 to 12
Cortisone acetate	25	0.8	8 to 12
Intermediate acting			
Prednisone	5	4	12 to 36
Prednisolone	5	4	12 to 36
Methylprednisolone	4	5	12 to 36
Triamcinolone	4	5	12 to 36
Long acting			
Dexamethasone	0.75	30	36 to 72
Betamethasone	0.6	30	36 to 72

Antibiotic Treatment Options in COPD Exacerbation

- Empiric antibiotic regimens should target the most common bacterial pathogens in COPD:
 - (1) *Haemophilus influenzae*
 - (2) *Streptococcus pneumoniae*
 - (3) *Moraxella catarrhalis*
- Antibiotic coverage for *Pseudomonas aeruginosa* is indicated in patients with risk factors and patients who don't respond to empiric treatment.
 - Risk factors for *Pseudomonas* include: history of *Pseudomonas* infections, FEV₁ < 50% of predicted, recent hospitalization, more than 3 courses of antibiotics within the past year, use of systemic corticosteroids.

Empiric Antibiotic Treatment of COPD Exacerbation in Hospitalized Patients (UpToDate)



A respiratory quinolone like levofloxacin has enhanced Gram positive coverage for *Streptococcus pneumoniae*.

Antipseudomonal Antibiotics

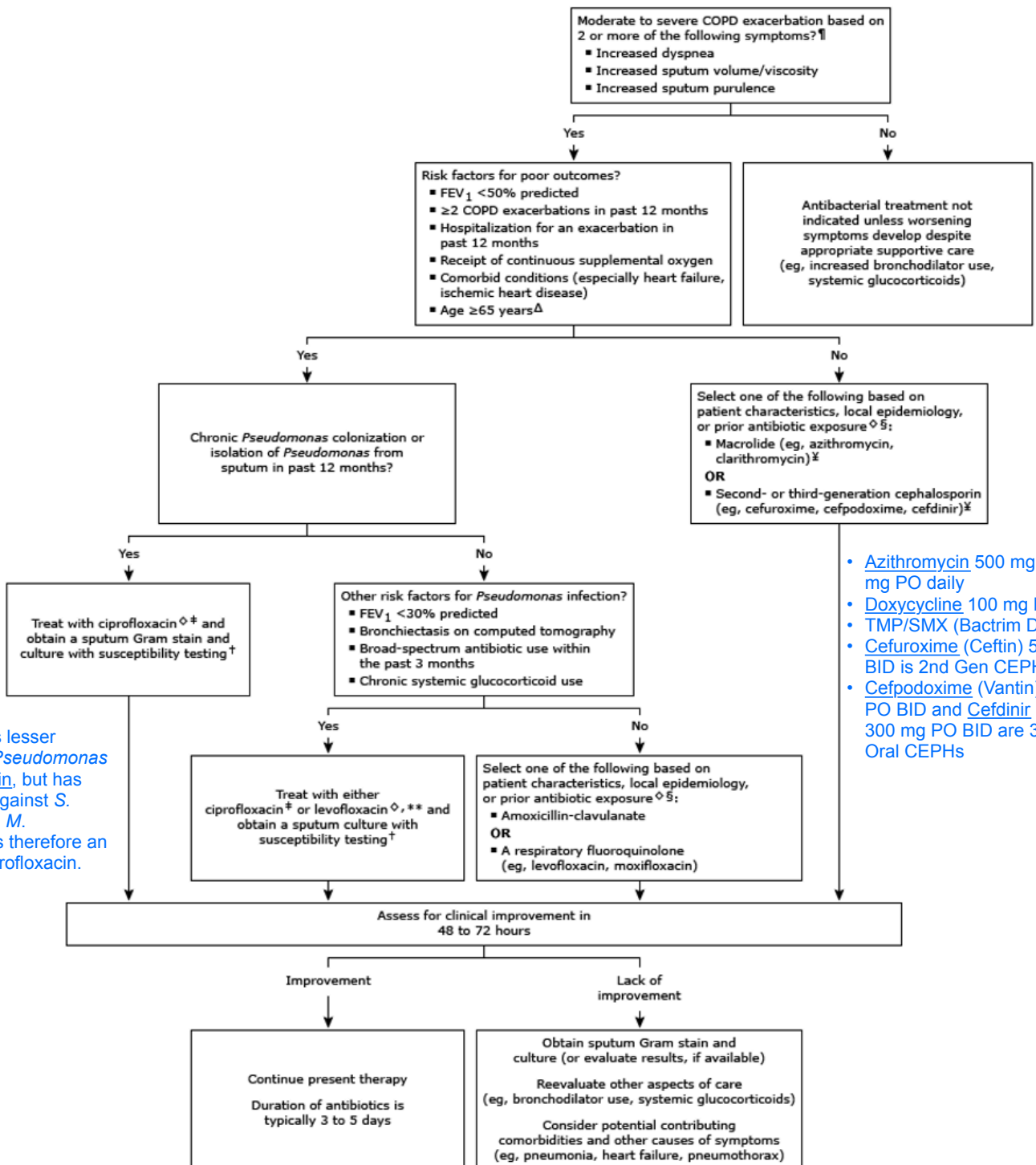
- Ceftazidime (3rd Gen CEPH)
- Cefepime (4th Gen CEPH)
- Piperacillin/Tazobactam (Zosyn) (Anti-Pseudomonal Penicillin)
- Quinolones: Levofloxacin & Ciprofloxacin
- Carbapenems: Meropenem & Ertapenem
- Aminoglycosides: Gentamicin & Tobramycin
- Aztreonam

Ceftriaxone (Rocephin) & Cefotaxime (Claforan) are 3rd Gen CEPHs

Note: The FEV₁ is used to classify the severity of obstructive lung diseases traditionally based on % predicted values into five levels: FEV₁ >70% of predicted is mild. FEV₁ 60-69% of predicted is moderate. FEV₁ 50-59% of predicted is moderate-severe. FEV₁ 35-49% of predicted is severe.

Empiric Oral Antibiotic Treatment Regimens COPD Exacerbation in Outpatients

- The choice of antibiotics depends on community bacterial resistance patterns and individual risk of *Pseudomonas aeruginosa*, such as FEV₁ < 50% of predicted, recent hospitalization, more than 3 courses of antibiotics within the past year, use of systemic corticosteroids.
- Empiric antibiotic regimens (3-5 days) should target the most likely bacterial pathogens in COPD: *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*.



Long-Term Antibiotic Prophylaxis in Severe COPD

- Patients with severe COPD with ≥ 2 exacerbations/year despite optimal medical management may benefit from prophylactic macrolide therapy:
 - Azithromycin 250-500 mg PO three times weekly
- Patients on long-term prophylactic macrolide therapy should be monitored closely for development of antimicrobial resistance, QT-interval prolongation, and *Clostridium difficile* infection.