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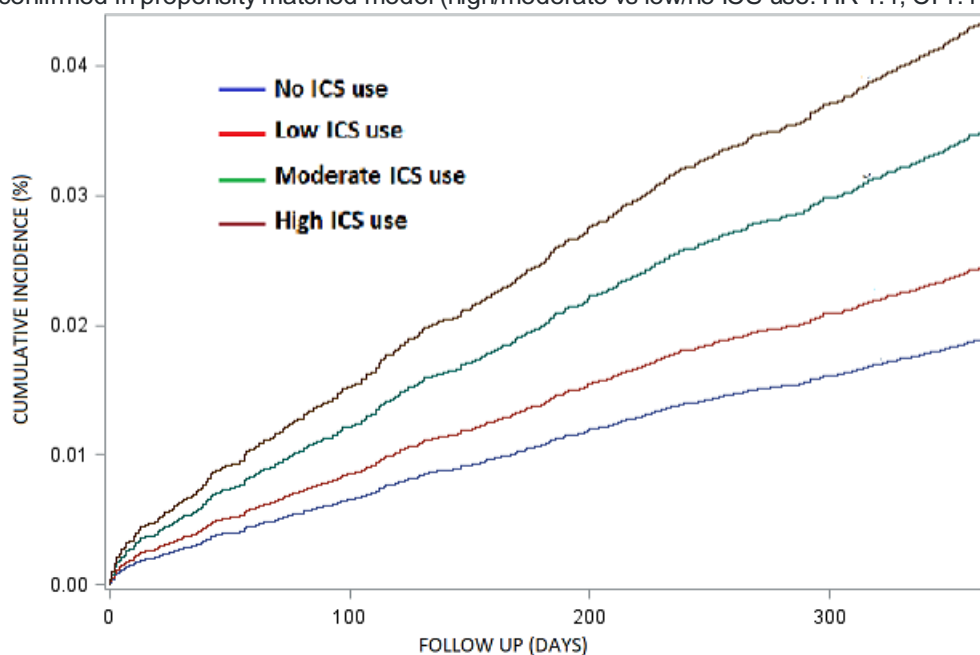
Risk of *Haemophilus Influenzae* Infection in Patients with Chronic Obstructive Pulmonary Disease Using Inhaled Corticosteroids: A Cohort Study of 23,789 Outpatients.

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Inhaled corticosteroids (ICS) are widely used in chronic obstructive pulmonary disease (COPD) treatment, despite known risk of pulmonary infections. We investigated the risk of acquiring a *Haemophilus influenzae* (HI) positive airway culture in ICS users, by conducting an epidemiological cohort study from 1.1.2010 to 18.2.2018, including 23,789 Danish COPD outpatients.

ICS use 365 days prior to cohort entry was categorised into low, moderate, and high based on accumulated ICS dose extracted from reimbursed prescriptions. Cox proportional hazards regression model was used to assess the future risk of acquiring HI within 365 days from cohort entry and sensitivity analyses were done using propensity score matched models.

670 (2.8%) patients acquired HI during follow-up. Use of ICS was associated with dose dependent increased risk of acquiring HI (low dose: Hazard Ratio (HR) 1.3, 95% confidence interval (CI) 1-1.7, p-value (p)=0.02; moderate dose: HR 1.9, CI 1.5-2.4, p<.0001; High dose HR 2.4 CI 1.9-2.9 p<.0001 reference: no ICS use). Results were confirmed in propensity matched model (high/moderate vs low/no ICS use: HR 1.4, CI 1.44-1.44, p<.0001).



Cumulative incidence, in percentage (%), of *Haemophilus Influenzae* during first 365 follow-up days after cohort entry, categorised according to different accumulated doses of ICS.

So ICS use in COPD outpatients was associated with significant dose dependent increase in risk of acquiring *HI*.
Clinical assessment of benefits vs risk of infection should be made before prescription of ICS.

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