Introduction:
Limited recommendations exist regarding evaluation, prevention and treatment of withdrawal syndromes in both pediatric and adult ICU populations. Given the potential for complications and its iatrogenic nature, defining the syndrome and identifying patients at risk is important. We conducted a systematic review to examine the frequency of withdrawal, risk factors and symptoms of iatrogenic withdrawal in critically ill pediatric and adult patients who received benzodiazepines and/or opioids during their ICU stay.

Methods:
The literature search was conducted in Pubmed, Medline, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane register of systematic reviews, DARE, CINAHL, Trip database, CMA infobase and NICE evidence from inception to October 2017. We also examined the grey literature. We included studies reporting frequency, risk factors or symptomatology of iatrogenic withdrawal of opioids, benzodiazepines (or both) in critically ill patients. We considered all study designs except case reports and case series. Pairs of reviewers independently abstracted data and evaluated methodological quality using the Cochrane collaboration tool, Newcastle-Ottawa or QUADAS-2. PROSPERO (registration number: CRD42016042746).

Results:
We identified 21210 unique citations through database search and 146 full-texts were assessed for eligibility. Thirty-three studies were included; the majority were observational and only a few included adults. In prospective studies, mixed withdrawal was observed in 16.7% of adults and ranged from 7.5% to 100% in pediatric studies. Symptoms of withdrawal were not well described. Risk factors included higher cumulative dose and prolonged administration of opioids and benzodiazepines.

Conclusion:
Iatrogenic withdrawal appears to be a frequent syndrome in critical care patients who received infusions of opioids and/or benzodiazepines. Larger studies are required, especially in critically ill adults, to better define the syndrome and its symptomatology.