

Supplementary File S4: Definitions of opioid induced respiratory depression in the studies

Study ID	Definition of the Respiratory depression in the individual studies
¹⁴ Etches et al. ¹⁹⁹⁴	Naloxone for reversal of opioid induced RD (unresponsive, cyanosis, desaturation, RR 4-8/min, PaO ₂ < 80mmHg, PaCO ₂ >55 mmHg, excessive sedation, confusion, upper airway obstruction)
¹² Gordon et al. ²⁰⁰⁵	Naloxone for SpO ₂ <90%, excessive sedation, hypotension, other side effects
¹¹ Shapiro et al. ²⁰⁰⁵	Whenever RR < 10 /min; nurses performed following event-response algorithm: discontinue analgesia delivery system, administer 100% oxygen, and inform treating surgeon or anesthesiologist. Whenever RR < 8 /min, naloxone (0.1 mg in 50 mL saline) was added to above algorithm
¹³ Taylor et al. ²⁰⁰⁵	RE was defined as RD (< 10 /min) and/or a decrease in SpO ₂ (< 90%) during narcotic administration in postoperative period, that was reversed by naloxone.
¹⁰ Overdyk et al. ²⁰⁰⁷	Oxygen desaturation or bradypnea had to be sustained below threshold for ≥ 3 min with mean SpO ₂ < 90% or RR < 10/min.
⁹ Ramachandran et al. ²⁰¹¹	Opioid-related LT-CRE was defined as an unresponsive and hypoxic or apneic patient needing rescue medical therapy with naloxone during concurrent opioid therapy.
⁷ Khelemsky et al. ²⁰¹⁵	Administration of naloxone within first 72h in postoperative period
⁸ Lee et al. ²⁰¹⁵	Criteria for definitive RD were: (1) patient received naloxone and showed evidence of reversal of RD, or (2) other clear and objective signs of RD or opioid toxicity, for example constellation of clinical signs such as over-sedation, respiratory arrest, and need for resuscitation. Criteria for probable RD were: (1) RR < 8/min, (2) somnolence, (3) SpO ₂ < 90% in absence of abnormal baseline SpO ₂ (4) pinpoint pupils, (5) administration of high doses of opioids in opioid-naive patient, or (6) qualitative observation of RD (e.g. snoring, airway obstruction, or cyanosis) that required intervention (e.g. jaw lift, positive pressure mask ventilation, or intubation). The criterion for possible RD was a patient found in cardiopulmonary arrest without another identified cause (e.g. pulmonary embolism or neuraxial cardiac arrest) and with a presumed risk for RD (e.g. obese patient receiving significant amounts of opioids, history of snoring, loud breathing, or somnolence).
⁶ Weingarten et al. ²⁰¹⁵	Naloxone to reverse OIRD or sedation within 48h after discharge from anesthesia care for adverse respiratory events [hypoventilation < 8 breaths/ min, apnea, oxyhemoglobin desaturation, pain/sedation mismatch].
⁵ Weingarten et al. ²⁰¹⁵	Apnea, hypopnea, oxyhemoglobin desaturations, or episodes of severe pain despite moderate to profound sedation.
³ Rosenfeld et al. ²⁰¹⁶	A drug-related adverse event was identified when a patient was administered opioid ≤ 24h prior to naloxone administration.
⁴ Weingarten et al. ²⁰¹⁶	Naloxone within 48 h of dismissal from anesthetic care (dismissal from PACU or transfer from operating room to postoperative area [i.e., postsurgical ward, ICU, progressive care unit]).

RD – respiratory depression, RR- respiratory rate, PACU- post-anesthesia care unit, ICU- intensive care unit, RE- respiratory event, LT-CRE- life-threatening critical respiratory event