

Year	Milestone / Study	Significance
1959	Avery & Mead identify surfactant deficiency	Established pathophysiology of neonatal RDS
1971	Gregory introduces CPAP	Provided non-invasive alternative to intubation
1980	Fujiwara's first clinical surfactant trial	Demonstrated efficacy of natural surfactant in preterm infants
1980s–1990s	RCTs and FDA approvals	Surfactant therapy becomes standard of care (product approvals in early 1990s)
1990s	Natural vs. synthetic surfactant trials	International trials show animal-derived surfactants improve outcomes
Mid-1990s	Early-rescue dosing strategy	Shift from prophylactic to selective surfactant administration (global adoption)
Late 1990s	INSURE technique introduced	Intubate–Surfactant–Extubate reduces ventilation exposure
2008	COIN Trial	Supports CPAP-first approach over routine intubation
2010	SUPPORT Trial	Confirms CPAP-first with selective surfactant as safe and effective
2007–2013	LISA/MIST techniques emerge	Thin-catheter surfactant delivery on CPAP; early less-invasive methods validated
2014–2021	OPTIMIST-A and related trials	Evaluates minimally invasive surfactant therapy in extremely preterm infants (protocol 2014, results 2021)
2019–2024	Aerosolized and LMA surfactant delivery	Investigates non-ETT routes to further reduce invasiveness
2020	Aerosolized Calfactant RCT	Reduced intubation need; proof-of-concept for non-invasive surfactant delivery
2021	OPTIMIST-A primary results	Reduced ventilation exposure but no difference in primary outcome
2023	Neo-INSPIRe Trial Launch	Large multicentre RCT testing aerosolized surfactant in preterm infants
2023	NRP/AHA Guideline Update	Reinforces CPAP-first and selective surfactant; supports non-invasive techniques
2024	LISA vs INSURE Umbrella Review	Confirms LISA superiority for reducing ventilation, BPD, and death
2025	SALSA Guidelines for LMA Surfactant	Standardized LMA surfactant administration expands non-invasive options