QUESTION

Should ETT s analysis?	uction vs. No ETT suction be used for non-vigorous infants: a systematic review and meta-
POPULATION:	Non-vigorous infants delivered through meconium-stained amniotic fluid :a systematic review and meta-analysis
INTERVENTION:	ETT suction
COMPARISON:	No ETT suction
MAIN OUTCOMES:	Survival at discharge; Survival at discharge (obs); Mental neurodevelopmental impairment; Motor neurodevelopmental impairment; Hypoxic ischemic encephalopathy; Hypoxic ischemic encephalopathy (obs); Meconium aspiration syndrome; Meconium aspiration syndrome (obs); Mechanical ventilation; Mechanical ventilation (obs); Respiratory support (excluded mechanical ventilation); DR interventions - ETT for PPV; Delivery room interventions (chest compressions); Delivery room interventions (chest compressions) (obs); Delivery room interventions (epinephrine); Treatment of pulmonary hypertension (iNO, oral medications, ECMO); Length of hospitalization; Length of hospitalization (obs);
SETTING:	Delivery suites
PERSPECTIVE:	
BACKGROUND:	Up to 20% of all births are affected by meconium stained amniotic fluid. About 5% of those exposed to meconium stained amniotic fluid aspirate the fluid into their lungs resulting in significant illness after birth called Meconium Aspiration Syndrome (Wiswell 1993, 955; Singh 2009, 497). Infants born through MSAF who are nonvigorous represent 1.5% to 3% of all births. When contemplating the worldwide number of births, this question impacts significant number of babies annually (Almeida 2017, 576; Qian 2008, 1115; Bhat 2008, 199). The controversy around the 2015 recommendation for abandoning routine endotracheal suctioning continues to rage, as evidenced by recent randomized trials (Chettri 2015, 1208, Nangia 2016, 79, Singh 2018) and one retrospective study (Chirovolu 2018). Current practice in caring for newborns delivered through meconium-stained amniotic fluid includes immediate resuscitation without laryngoscopy, immediate laryngoscopy with subjective determination of need for tracheal suctioning and immediate laryngoscopy with tracheal suctioning.
CONFLICT OF INTERESTS:	Authors declare they have not conflicts of interest.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 No Probably no Probably yes Yes Varies Don't know 	Up to 20% of all births are affected by meconium stained amniotic fluid. About 5% of those exposed to meconium stained amniotic fluid aspirate the fluid into their lungs resulting in significant illness after birth called Meconium Aspiration Syndrome (Wswell 1993, 955; Singh 2009, 497). Infants born through MSAF who are non-vigorous represent 1.5% to 3% of all births. When contemplating the worldwide number of births, this question impacts significant number of babies annually (Almeida 2017, 576; Qian 2008, 1115; Bhat 2008, 199). The controversy around the 2015 recommendation for abandoning routine endotracheal suctioning continues to rage, as evidenced by recent randomized	

	trials (Chettri 2015, 1208, Nangia 2016, 79, Singh 2018) and one retrospective study (Chirovolu 2018). Current practice in caring for newborns delivered through meconium-stained amniotic fluid includes immediate resuscitation without laryngoscopy, immediate laryngoscopy with subjective determination of need for tracheal suctioning and immediate laryngoscopy with tracheal suctioning.	
Desirable Effects How substantial are the desirable anti	cipated effects?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Trivial Small Moderate Large Varies Don't know 	Severe asphyxia is a common condition in non-vigorous infants delivered through meconium-stained amniotic fluid. Initiating ventilation within the first minute of life in non-breathing or ineffectively breathing infants is strongly recommended. Delay in initiating ventilation, especially where the provider is unable to promptly intubate the infant or suction attempts are repeated, may negatively impact critical outcomes (i.e. survival, long-term neurodevelopmental outcomes). On the other hand, elective suctioning of the upper airways could reduce incidence and severity of the respiratory disease (MAS). If there was a finding of benefit of the intervention, this could be a large benefit for the individual, family, and population. However, our review of the intervention, this could lead to large degree of harm for the individual, family, and population. However, four on significant concern for harm of the intervention.	
Undesirable Effects How substantial are the undesirable a	nticipated effects?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Large Moderate Small Trivial Varies Don't know 	Severe asphyxia is a common condition in non-vigorous infants delivered through meconium-stained amniotic fluid. Initiating ventilation within the first minute of life in non-breathing or ineffectively breathing infants is strongly recommended. Delay in initiating ventilation, especially where the provider is unable to promptly intubate the infant or suction attempts are repeated, may negatively impact critical outcomes (i.e. survival, long-term neurodevelopmental outcomes). On the other hand, elective suctioning of the upper airways could reduce incidence and severity of the respiratory disease (MAS). If there was a finding of benefit of the intervention, this could be a large benefit for the individual, family, and population. However, our review of the intervention, this could lead to large degree of harm for the individual, family, and population. However, four no significant concern for harm of the intervention.	
Certainty of evidence What is the overall certainty of the evid	dence of effects?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

 Very low Low Moderate High No included studies 	The certainty of evidence was low for the primary outcome (survival at discharge) and ranged from very low to low for secondary outcomes (neurodevelopmental impairment, incidence of MAS, need for intubation, chest compressions and medications in delivery room, duration of hospital stay, etc).	
Is there important uncertainty about o	r variability in how much people value the main outcomes?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Important uncertainty or variability Possibly important uncertainty or variability Probably no important uncertainty or variability No important uncertainty or variability 	Despite available studies that were considered to have a high risk of bias, and the certainty of evidence ranged from low to very low for the considered outcomes, the taskforce considers that there is probably no important uncertainty or variability in how much people value the main outcomes.	
Balance of effects Does the balance between desirable a	nd undesirable effects favor the intervention or the comparison?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Favors the comparison Probably favors the comparison Does not favor either the intervention or the comparison Probably favors the intervention Favors the intervention Varies Don't know 	The taskforce places value on both harm avoidance (delays in providing bag- mask ventilation, potential harm of the procedure) and the unknown benefit of the intervention of routine laryngoscopy with or without tracheal intubation and suctioning. Routine practice of this intervention for non-vigorous infants is more likely to result in delays in initiating ventilation, especially where the provider is unable to promptly intubate the infant or suction attempts are repeated. In the absence of evidence of benefit for suctioning, the emphasis should be on initiating ventilation within the first minute of life in non-breathing or ineffectively breathing infants.	
Resources required How large are the resource requirement	ents (costs)?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

 Large costs Moderate costs Negligible costs and savings Moderate savings Large savings Varies Don't know Certainty of evidence of the second s	Routine practice of laryngoscopy with or without tracheal intubation and suctioning would require increased personnel, training, and equipment. Therefore, there would be potentially moderate savings in costs for not routinely performing the intervention. On the other hand, equipment for suctioning and intubation and trained personnel should be available at every delivery (independently from the presence of meconium stained amniotic fluid).	
What is the certainty of the evidence o	f resource requirements (costs)?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Very low Low Moderate High No included studies 	The costs were not reported in the included studies. However, as the critical outcomes (survival at discharge, NDI, MAS) and the important outcomes (i.e. need for ventilation, treatment of pulmonary hypertension, duration of hospitalization) were similar between intervention and comparison group, the certainty of the evidence of the required resources seems to be moderate.	
Cost effectiveness Does the cost-effectiveness of the inte	ervention favor the intervention or the comparison?	
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
 Favors the comparison Probably favors the comparison Does not favor either the intervention or the comparison Probably favors the intervention Favors the intervention Varies No included studies 	The critical outcomes (survival at discharge, NDI, MAS) and the important outcomes (i.e. need for ventilation, treatment of pulmonary hypertension, duration of hospitalization) were similar between the intervention and comparison group. As the intervention group would require more equipment use, the cost-effectiveness probably favors the comparison group.	

Equity What would be the impact on health equity?							
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS					
 Reduced Probably reduced Probably no impact Probably increased Increased Varies Don't know 	In low-resource settings, equipment and adequately trained personnel to perform the intervention are not always available. An intervention that does not include direct laryngoscopy with or without tracheal intubation and suctioning is more likely to increase health equity globally, including in low- resource settings where the largest incidence of non-vigorous infants delivered through meconium-stained amniotic fluid occurs.						
Acceptability Is the intervention acceptable to key s	takeholders?						
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS					
 No Probably no Probably yes Yes Varies Don't know 	The intervention is acceptable to key stakeholders.						
Feasibility Is the intervention feasible to impleme	ent?						
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS					
 No Probably no Probably yes Yes Varies Don't know 	From a practical point of view, avoiding routine laryngoscopy with or without tracheal intubation and suctioning is feasible and easy to implement. Despite new studies that have become available after the 2015 recommendation, this review shows that the certainty of evidence remains low or very low. However, the uncertainty of these results could limit the implementation of the recommendation among clinicians.						

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know

CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	lmportant uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the	Conditional recommendation for the intervention	Strong recommendation for the intervention
		comparison		
0	•	0	0	0

CONCLUSIONS

Recommendation

For non-vigorous newborns delivered through meconium-stained amniotic fluid, we suggest against routine immediate direct laryngoscopy after delivery with or without

tracheal suctioning when compared to immediate resuscitation without direct laryngoscopy. Meconium-stained amniotic fluid remains a significant risk factor for receiving advanced resuscitation in the delivery room. Rarely, an infant may require intubation and tracheal suctioning to relieve airway obstruction.

Justification

Overall justification

The Task Force recognizes that, while the Treatment Recommendation has not changed, several studies have been added to the literature since the last recommendation was made. While these studies contribute new evidence regarding this topic, the certainty of the findings remains low or very low due to the difficulty of performing unbiased studies of this clinical guestion as well as failure of the data to reach optimal information size.

In making this suggestion, we place value on both harm avoidance (delays in providing bag-mask ventilation, potential harm of the procedure) and the unknown benefit of routine tracheal intubation and suctioning.

Routine suctioning of non-vigorous infants is more likely to result in delays in initiating ventilation, especially where the provider is unable to promptly intubate the infant or suction attempts are repeated. In the absence of evidence of benefit for routine suctioning, the emphasis should be on initiating ventilation within the first minute of life in non-breathing or ineffectively breathing infants born through meconium-stained amniotic fluid. Some newly born infants may receive tracheal intubation in order to clear a blocked airway or for subsequent ventilation (Edwards 2019 E68, Kalra 2019).

Detailed justification

Undesirable Effects

The Taskforce considered the potential for harm in the procedure of endotracheal intubation and the delay of positive pressure ventilation with the intervention, for which there was no evidence of benefit.

Certainty of evidence

The certainty of evidence for benefit of the intervention remained low to very low.

Values

The Taskforce considered that the procedure of laryngoscopy with or without tracheal intubation and suctioning is invasive and has potential for harm. The context of no evidence for benefit led to the suggestion against routine practice of the intervention. While immediate intubation and tracheal suctioning after birth is not routinely suggested, the likelihood of intubation for resuscitation remains a strong possibility. Therefore, trained personnel and equipment for intubation should be readily available for deliveries where meconium stained amniotic fluid is present. This includes the potential use of a meconium aspirator after intubation, as in cases of airway obstruction, where the only means of relieving the obstruction could be tracheal suctioning.

Subgroup considerations

The criteria for subgroup analyses were not met.

Implementation considerations

Implementation will not require further equipment or resources compared to current practice. There may be a decrease in use of equipment due to reduced use of supplies for laryngoscopy, intubation, and suctioning. However, there will not be reduced need for personnel or training. Meconium stained amniotic fluid is a risk factor for receiving advanced neonatal resuscitation. Therefore, appropriate personnel and equipment should always be available.

Monitoring and evaluation

As practice recommendations have changed over the past two decades, and there are no current large clinical trials to inform this question for which there is no evidence of benefit, continued monitoring and evaluation is highly recommended.

Research priorities

Despite the addition of several randomized trials focused on this clinical question, the optimal information size is not achieved even with all of the studies taken together. The difficulties of performing a study while minimizing the risks of bias due to difficulty with blinding and assessment of outcome make accrual of evidence a significant challenge. The priorities for study remain similar to previous versions of the CoSTR:

- Does the potential for harm (i.e. delay in starting positive pressure ventilation or transient bradycardia/hypoxia, mortality, NDI) outweigh the potential for benefit (i.e. reduction of MAS, need for mechanical ventilation or treatment of pulmonary hypertension)?
- Do risks or benefits of intubation with tracheal suctioning vary with any subgroup (gestational age, thickness of meconium, operator experience)?
- Long-term outcomes should be included in future studies.
- The neurodevelopmental, behavioural, or educational assessment for future studies should be at or after 18 months of age and completed with a validated tool.