Resuscitation of Preterm Infants in Low and Middle-Income Countries **AN ETHICAL ANALYSIS**



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BACKGROUND

- Preterm birth is a leading cause of mortality and morbidity for newborn infants. Resuscitation is often possible, yet is costly and associated with complications.
- Each year, approximately 780,000 infants are born *extremely* preterm (<28 weeks gestation), the majority of which are in Low and Middle-Income Countries (LMICs) where limits on resources may impact the provision of medical care.
- In High-Income Countries (HICs), management guidelines exist about when resuscitation of Extremely Preterm Infants (EPIs) should be provided (Fig 1).
- In LMICs, such guidelines do not exist. In part, due to the lack of guidance, there is significant variation within countries as to the resuscitation thresholds used by



clinicians (Fig 2). In these settings, relevant ethical guidance does not exist for clinicians making complex decisions involving poverty, disability and resource scarcity.



RESEARCH QUESTION

"How should clinicians make decisions about resuscitation of extremely preterm infants (EPIs) in low and middle-income countries (LMICs)?"

B: ADAPTING PROGNOSIS-BASED GUIDELINES CURRENTLY USED IN HIGH-INCOME COUNTRIES PART

- Based upon the **ethical principle of consistency**, existing prognosis-based guidelines were adapted for use in LMICs.
- A new framework the Weight And Gestation Equivalent mortality framework (WAGE) – was developed, capable of integrating limited data available from neonatal intensive care units (NICUs) in the Philippines.
- Under this framework, mortality-based thresholds for resuscitation were derived from finding equivalent mortality rates to prognostic categories used in HICs.
- Thresholds were applied to data on mortality for different categories of combined gestational age/birthweight in the Philippines.
- Using these two variables, clinicians may classify infants into different treatment categories shortly after delivery, based on their estimated mortality rate (Fig 3).

	Mortality Rates				Treatment Category:
GA BW	<28	28-32	33-36	Term	Mortality rate >80% - <u>Treatment not indicated</u> (Life sustaining treatment should not usually be provided)
<500g	100%	100%	N/A		
500-749g	80.1%	68.7%	N/A		Mortality rate 40,80% · Treatment entional
750-999g	85.0%	65.1%	48.7%		(Life sustaining treatment should be guided by parents' wishes)
1000-1249g	66.7%	45.5%	N/A		
1250-1499g	31.8%	35.3%	25.%		Mortality rate <40%: <u>Treatment indicated</u> (Life sustaining treatment should usually be provided)
1500-1749g	23.1%	19.5%	5.6%		

Fig 3: The WAGE Framework applied to data from the Philippines.

METHODOLOGY

- An ethical analysis was conducted, combining ethical theory with pragmatic **considerations.** This attempted to address a series of ethical questions that are central to decisions around resuscitation of EPIs in LMICs.
- Ethical reasoning was applied to the **Republic of the Philippines** as a case-study, incorporating and extrapolating data supplied from the Philippine General Hospital, Manila.
- From here, a generic step-by-step paradigm was developed for clinicians wishing to develop guidelines in other LMIC settings.

PART A: ATTEMPTING TO CONSTRUCT GUIDELINES USING A COST-EFFECTIVENESS ANALYSIS (CEA)

- This method aims to inform clinicians of a gestational age (GA) prior to which resuscitation *should not be provided* as the opportunity costs are too large.
- It was ultimately rejected based upon epistemic uncertainty relating to: (1) Insufficient data on costs and outcomes of preterm birth from the Philippines; (2) The amount we ought to allocate to neonates (i.e. the 'cost-effectiveness' threshold' or 'CET') based upon the moral status of newborns.

Can we use imported data?

Conclusions vary significantly if data is sourced from analyses conducted in HICs or LMICs.

How much should we allocate?

• The World Health Organisation (WHO) recommends investing in interventions when the cost/DALY averted is less than the GDP/capita.

PART C: PRACTICAL CONSIDERATIONS IN THE IMPLEMENTATION OF THE WAGE FRAMEWORK

- It would be most appropriately employed through a national workshop of relevant professionals.
- The workshop should allow for revisions to be made to the framework.
- In many LMICs, there is a large degree of heterogeneity **between private and public sectors.** The optional nature of private care and the possibility of transfers suggests differences in the application of WAGE in each sector.
- When applied to both private and public hospitals within the same region, upper thresholds (of mandatory resuscitation) ought to be consistent, whereas lower thresholds (of withholding resuscitation) may differ (Fig 4).



Fig 4: Different thresholds used in private/public sectors

CONCLUSIONS: A STEP-BY-STEP PROCESS FOR CLINICIANS WISHING TO CONSTRUCT GUIDELINES IN LIMICS

Step 1: Assess the appropriateness of providing or scaling up newborn intensive care. Investing in NICUs is recommended if the NMR has been reduced to <15 through public health measures.

> Step 2: Collect preliminary data. Data on mortality rates relative to both GA and birthweight.

Step 3: Gather together the relevant expertise for a national workshop. Primarily medical professionals but may also include input from other stakeholders.



- Data imported from the UK suggests that resuscitation should not be provided prior to 34 weeks GA. However, extrapolating data across regions with differing levels of income is likely to produce unreliable results.
- Only one CEA has been conducted in a LMIC (Mexico) on resuscitation of EPIs. Data applied to the Philippines from this study suggests that resuscitation should be provided at all gestational ages. This analysis however, imported large amounts of data from HICS, with multiple assumptions made in its application to Mexico.
- Results vary significantly depending on the assumptions made in importing data from HICs to LMICs.
- Conclusions also vary if a different costeffectiveness threshold (CET) is used for neonates.

- This may not apply for neonates depending on one's view of the moral status of newborns:
- Implications for conducting a cost-Moral effectiveness analysis in resource-poor Status of Neonate settings
 - Using only *parental* quality of life in
- No moral calculating QALYS or DALYs.
- Redirecting funds to older children with status an interest in continued life.
- Countries will need to discount their CET Gradualist relative to the development of the accounts neonate.
- CEA conducted in the same manner as other children/adults. Full moral
- Redirecting funds from older individuals status toward NICUs.

Step 4: Draw upon models being currently used elsewhere – The WAGE Framework.

Step 5: Establish regionally uniform upper thresholds across private and public sectors.

Step 6: Consider revisions to framework and attempt to reach reflective equilibrium.

Step 7: Review process over time as further data is collected.

The WAGE Framework represents a stepping-stone toward a more sophisticated prognosis-based guideline, enabling greater consistency of care for patients, and providing ethical guidance for clinicians making decisions about resuscitation of EPIs in LMICs.

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