Differentiating mortality risk of individual infants and children to improve survival: opportunity for impact

James A Berkley, Judd L Walson*, Rajiv Bahl, Nigel Rollins*

Children are not born equal in their likelihood of survival. The risk of mortality is highest during and shortly after birth. In the immediate postnatal period and beyond, perinatal events, nutrition, infections, family and environmental exposures, and health services largely determine the risk of death. We argue that current public health programmes do not fully acknowledge this spectrum of risk or respond accordingly. As a result, opportunities to improve the care, survival, and development of children in resource-poor settings are overlooked. Children at high risk of mortality are underidentified and commonly treated using guidelines that do not differentiate care according to the magnitude or drivers of those risks. Children at low risk of mortality are often provided with more intensive care than needed, disproportionately using limited health-care resources with minimal or no benefits. Declines in newborn, infant, and child mortality rates globally are slowing, and further reductions are likely to be incrementally more difficult to achieve once simple, high impact interventions have been universally implemented. Currently, 63 countries have rates of neonatal mortality that are off track to meet the Sustainable Development Goal 2030 target of 12 deaths per 1000 livebirths or less, and 54 countries have rates of mortality in children younger than 5 years that are off track to meet the target of 25 deaths per 1000 livebirths or less. If these targets are to be met, a change of approach is needed to address infant and child mortality and for health-care systems to more efficiently address residual mortality.

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*Contributed equally as first authors

Kenya Medical Research Institute, Wellcome Trust Research Programme, Kilifi, Kenya (Prof J A Berkley FMedSci); **Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK** (Prof J A Berkley); **Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA** (Prof J L Walson MD); **Department of Maternal, Newborn, Child and Adolescent Health and Ageing, WHO, Geneva, Switzerland** (R Bahl PhD, N Rollins MD); **India Council of Medical Research, New Delhi, India** (R Bahl)

Correspondence to: Nigel Rollins, Department of Maternal, Newborn, Child and Adolescent Health and Ageing, WHO, Geneva 1211, Switzerland **rollinsn@who.int**

The WHO Integrated Management of Childhood Illness and Integrated Community Case Management charts and algorithms are designed for, and widely used by, primary health-care workers in low-resource settings. These tools currently classify children who are unwell on the basis of disease severity, stratified by age;[1,2] care pathways for children without significant health conditions are coloured green, care pathways for infants and children with conditions associated with moderate risk are coloured yellow, and conditions associated with high, immediate risk of mortality are coloured pink. For example, the recommended management of children with severe acute malnutrition (SAM) is determined by simple anthropometric cutoffs and differs depending on whether children are classified as having complicated SAM or uncomplicated SAM, established by detecting the presence of other illnesses or the inability to adequately feed.[3]

However, these and other care pathways are generally focused on narrowly defined criteria classifying the severity of conditions (eg, severe dehydration, severe pneumonia, or severe anaemia) rather than classification of the overall risk faced by the individual infant or child. Hence, the recommended care pathway for an infant aged 9 months with a history of low birthweight, who is no longer breastfed, is unimmunised, or orphaned could be the same as for a child aged 3 years with normal birthweight and none of the other risks. This approach is neither effective nor efficient in ensuring that children at high risk of mortality receive the highest level of care available while avoiding unnecessary use of limited resources for children at low risk of mortality.

The effect of adverse birth outcomes, comorbidity, and undernutrition on newborn and child mortality is well recognised. In addition, the importance of maternal vital status and physical and mental health on child-health outcomes has also been highlighted.[4] Analyses have quantified risks associated with low birthweight, diarrhoeal disease, pneumonia, underweight, wasting, and stunting.[5,6] Yet, although these individual risks have been estimated for specific deficits or markers of severity within clinical syndromes, far less often has there been consideration of the interactions between multiple exposures nor their cumulative effect over time. Historical or environmental exposures including birth outcomes, disability, chronic comorbidities, poverty, food insecurity, and infant-feeding practices also clearly influence the likelihood of survival, development, and the lifelong wellbeing of infants and children (figure). These exposures affect mortality and health trajectories through shared pathways and, as a result, risk cannot be defined by exposure to just one category of risk.[7] Importantly, the effects of these exposures might also be indirect, additive, or multiplicative.

We propose that classifying children according to their individual mortality risk by assessing common exposures could readily be used programmatically to design and deliver differentiated support and management in both the community and in health-care facilities to protect against avertable morbidity and mortality. Such risk-differentiated care would enable health systems to more efficiently focus on infants and children at increased risk of mortality. Furthermore, by identifying children at decreased risk of mortality and delivering appropriate care and management, substantial financial and human resources could be redirected to children at high risk without negatively affecting outcomes among children at low risk.

The limitations of current risk classifications based on condition are illustrated by data from the CHAIN cohort

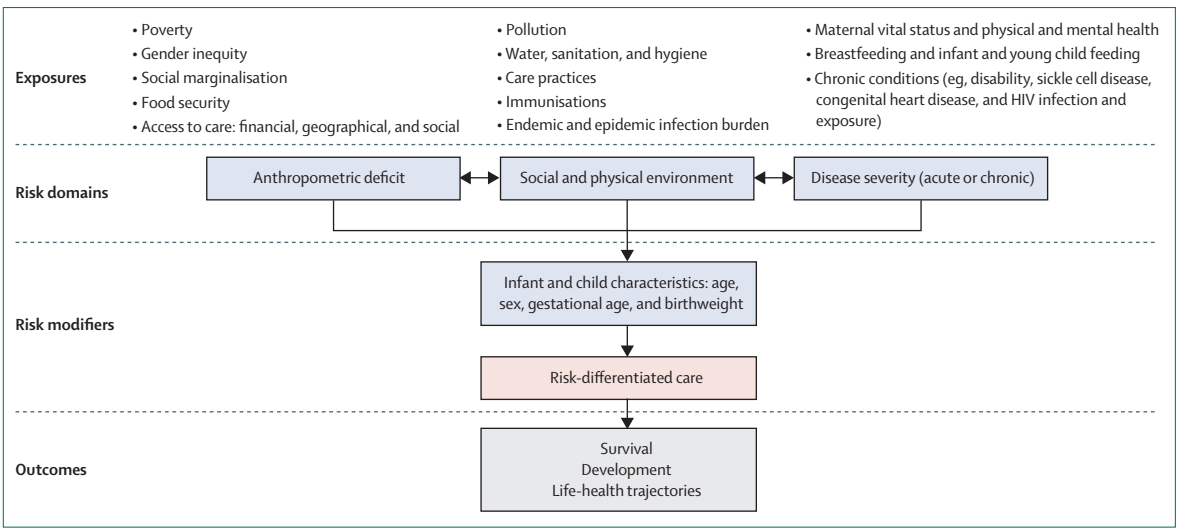

Figure: **Exposures that influence mortality, health, and development trajectories through shared pathways and opportunities for risk-differentiated care and support**

study[7] in Africa and south Asia and findings from analyses of the PREPARE dataset[8,9] that examined pneumonia-related mortality risks among young children in low-income and lower-middle-income countries. In the CHAIN cohort study, mortality was reported among children admitted to hospital with an acute illness where the quality of services in participating facilities to deliver interventions had been strengthened to meet or exceed national, local, or WHO guidelines. Despite children receiving recommended care and fulfilling standard discharge criteria, nearly half of the deaths among children presenting to hospital with acute illness occurred in the 6 months after discharge. Although the presenting condition had been treated, the underlying mortality risks of children had not been adequately addressed and in many cases were possibly not even recognised. The PREPARE analyses showed, in addition to disease-specific signs such as hypoxia and chest indrawing, that younger age, low weight-for-age, and female sex further increased the relative risk of dying.

What interventions, therefore, could mitigate vulnerabilities among children that are at high risk to further promote survival and optimal development? CHAIN[7] and PREPARE[8,9] show that managing children based on their presenting condition alone is not enough to fully address their respective risk and that additional approaches that go beyond individual conditions are needed. The studies ask the question: how do we efficiently identify marginalised families or families where the mother has not received formal education, has a mental or physical health problem, or has died, and intervene to mitigate risks?

In high-income settings, personalised medicine is a rapidly evolving principle of care.[10] In these settings, clinical care pathways that incrementally escalate or de-escalate treatment are commonly used in hospitals, and intensive care and trauma protocols routinely integrate risk assessments to inform next steps. Similarly, HIV programmes implement differentiated care according to individual characteristics and needs. However, in low-income countries, where infant, child, and maternal mortality remain high, information about underlying risk is not routinely used to guide support in the community, prevention, or treatment. Moving from public health population-based empirical management towards a targeted model that stratifies individual infants and children based on readily available predictors of risk, and provides management pathways accordingly, offers the potential to improve outcomes while reducing use of resources and costs to health services and, crucially, to families.

Furthermore, simple technologies, such as oxygen saturation monitoring, are already available to help health-care workers in low-resource settings to characterise which infants and children are at higher risk or lower risk of dying, but these technologies have not been effectively scaled up. The potential for risk-differentiated care to reduce mortality of children at high risk and improve the efficiency of health-system resources is eminently testable. Existing large datasets could be used to identify exposures, and identify maternal–child characteristics that could be implemented programmatically in different locations and health systems. Importantly, estimates of absolute risks and risk differences will be necessary to translate this knowledge into programmes. Point-of-care diagnostics, for example, might have the potential to further improve the precision of risk stratification and improve outcomes when coupled with appropriate clinical care and interventions, although further research is needed to show the utility of these approaches. Importantly, de-escalation of care for children at decreased risk of mortality could provide as much or more benefit to individuals and health systems as targeted escalation of treatment,

especially in light of antimicrobial resistance and costs associated with providing or receiving health care. Criteria could be developed to guide earlier discharge of children at decreased risk of mortality, and clinical care pathways could be revised and expanded to respond to the risk of the child beyond management of the presenting condition. It is important that appropriately designed and powered studies are conducted to assess mortality and cost–benefit outcomes of these interventional approaches.

Despite these opportunities, basic health-system challenges could restrict successful implementation. Simple, readily assessable, child-level characteristics such as age, birthweight, or current weight-for-age might not be collected because weighing scales are not consistently available or reliable; medical record systems might not be robust and information such as date of birth or birthweight might not be captured in home-based records, preventing basic health information from being available to families and health-care workers alike.

The WHO Risk Stratification Working Group has established a large pooled dataset[11] and completed an individual data analysis that estimates individual and accumulated risks of several child-level characteristics. This analysis,[12] along with other published reports[13,14] provide evidence that risk stratification can be undertaken in a variety of contexts. Although intervention trials are needed to establish the efficacy of risk-differentiated intervention packages, there is, even now, rationale for programmes to incorporate individual risk assessments and to identify infants and children at high risk of mortality. Once identified, these children can be prioritised for closer follow-up in the community and at health-care facilities to ensure high coverage of known effective interventions such as immunisations, breastfeeding, and counselling. Operational challenges can be identified; processes improved, documented, and reported; and lessons shared to improve scalability across many disparate health-care settings.

We have the opportunity to shift public health approaches towards more risk-informed management and efficient care. Health care is often described by the saying "every system is perfectly designed to get the results it gets".[15] We must therefore build on and revise health-care systems to ensure that they deliver what is needed to those who need it, without expending limited resources on those who are unlikely to benefit. In addition to developing and testing alternative management approaches, risk-differentiated care will require adaptations in thinking and meaningful shifts in health-care systems for effective programming to be in place by 2030. If the Sustainable Development Goal[16,17] targets are to be met, a change of approach is needed to address infant and child mortality and for health-care systems to more efficiently address residual mortality.

Contributors

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Declaration of interests

We decare no competing interests. The authors alone are responsible for the views expressed in this Viewpoint and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

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