Child Death Review Series III: Understanding why children die in high-income countries

Sidebotham P, Fraser J, Covington T, Freemantle J, Petrou S, Pulikottil-Jacob R, Cutler T, Ellis C,

Dr Peter Sidebotham, PhD
Associate Professor in Child Health
Division of Mental Health and Well Being
University of Warwick, Medical School Building, Coventry CV4 7AL, UK
p.sidebotham@warwick.ac.uk

Dr James Fraser, FRCPCH (corresponding author)
Consultant Paediatric Intensive Care
Bristol Royal Hospital for Children, Upper Maudlin Street, Bristol BS2 8BJ, UK
James.Fraser@UHBristol.nhs.uk

Theresa Covington, MPH
Director, National Center for the Review and Prevention of Child Deaths
c/o Michigan Public Health Institute
2455 Woodlake Circle Okemos, MI 48864, USA
tcovingt@mphi.org

Associate Professor Jane Freemantle, PhD
Principal Research Fellow
Centre for Health and Society, The Melbourne School of Population and Global Health
University of Melbourne
207 Bouverie St, Carlton, 3010, Australia
j.freemantle@unimelb.edu.au

Stavros Petrou, PhD
Professor of Health Economics
Warwick Clinical Trials Unit

University of Warwick, Medical School Building, Coventry CV4 7AL, UK
s.petrou@warwick.ac.uk

Ruth Pulikottil-Jacob
Research Fellow in Health Economics
Warwick Evidence
University of Warwick, Medical School Building, Coventry CV4 7AL, UK
R.Jacob@warwick.ac.uk

Tessa Cutler, Bsc
Research Assistant
Centre for Epidemiology and Biostatistics, The Melbourne School of Population and Global Health
University of Melbourne
207 Bouverie St, Carlton, 3010, Australia

Catherine Ellis, MSc
Senior Lecturer Adult & Children
Faculty of Health and Life Sciences
Coventry University, CV1 5FB, UK

Word count: 6201

Abstract

Through a structured narrative review of the literature, we have identified a wide range of factors influencing child and adolescent mortality in high income countries. These can be conceptualised within the four domains of intrinsic factors, the physical environment, the social environment, and service delivery factors. The most prominent factors in the literature are socio-economic gradients, although the mechanisms through which these gradients exert their effects are complex, affecting all four domains, and often poorly understood. While some factors are relatively fixed, including the child's gender, age, ethnicity and inherent genetic make-up, some parental characteristics, and some wider

environmental conditions, others may be amenable to interventions that could lessen risks and help to prevent future child deaths. A number of examples of systemic health service factors that may impact child survival are given, along with interventions such as modifications to the physical or social environmental that may impact more distal factors.

Introduction

The first two papers in this series provided an overview of the causes of child mortality in high income countries, focusing on data from the UK, USA, Australia and New Zealand, and setting these in a wider global context.[1, 2] The dramatic fall in child mortality in high income countries over the past century has been accompanied by changes in the causes and patterns of mortality. For example, in England and Wales, there were 16,909 deaths in children and young people aged 0-19 years in 1974. In 2012, this number had fallen to 4,909. However, such reductions have been most marked in younger age groups (Table 1), so that the highest mortality rates outside infancy are now found in adolescents. This shift reflects longer term epidemiologic changes across high income countries. The change in age distribution has been accompanied by changes in the relative contributions of different causes of death. External causes and unexplained deaths now account for 21% of deaths of children aged 1-14, compared to 32% in 1974. Conversely, perinatal and congenital causes now account for 24% of deaths in this age range compared to 15% in 1974, and acquired natural causes account for 66% of deaths compared to 53%. The reasons for theses shifts are complex and are likely to reflect both reductions in environmental risks as well as improvements in preventive and curative health care.

Table 1: Change in mortality, England and Wales, 1974 - 2012

Experience in child death review programmes in many countries has identified modifiable factors in children's deaths, highlighting that much could be done to further reduce child mortality. Whilst each individual child's death is a tragedy, it also provides an opportunity to learn and to potentially identify preventive work to protect other children. In order to achieve this however, we need to go deeper in our understanding, exploring the combination of factors that contributed to each child's death and interpreting those in the light of a wider knowledge base on factors contributing to child mortality.

In seeking to understand child development in the 1970s, Urie Bronfenbrenner argued that we can only fully understand a child's development by considering it within the context of the enduring environment within which he or she lives.[3] Bronfenbrenner and colleagues developed this as a bioecological model of development, recognising the interaction over time between the child and his or her environment.[4] The same principles apply in understanding child mortality. While we recognise, for example, that the meningococcus bacterium is a highly virulent organism, not all children who encounter it will die. The reasons some children succumb while others survive are complex and depend on the child's intrinsic resilience, factors in their physical and social environment, and in the care they receive. In this paper, we propose a framework for understanding the interaction of different factors contributing to child mortality. This framework, which draws on Bronfenbrenner's ecological principles, consists of four domains: factors intrinsic to the child; factors in the physical environment; factors in the social environment; and factors in relation to service provision. The framework has been developed by the authors, building on earlier work that informed the development of the child death review system currently used in England.[5] We use these four domains to explore the published literature on factors contributing to child mortality in high-income countries.

Methodology

A structured search strategy was developed and applied to each of the four domains. The search strategy (Panel 1) combined terms to identify published papers on child mortality, in high-income countries over the past 20 years. The search was limited to papers involving children, and a filter applied to include only papers on causation-etiology (McMaster Health Information Research Unit, Search Filters for MEDLINE in Ovid Syntax and the PubMed translation). This strategy was used to search for papers within Medline, and a modified form applied to the International Bibliography of the Social Sciences (IBSS), thus covering both medical and social sciences databases. The search terms used were intended to include papers relevant to infant, child, and adolescent mortality, but excluding fetal and maternal mortality. For the purposes of this review, we limited inclusion to studies arising in any of the 34 Organisation for Economic Co-operation and Development (OECD) member countries. As with previous papers in this series, we define a child as being from birth to

their 18th birthday, though recognise that some of the published literature uses different age ranges.

The baseline search was then combined with topic-specific searches in each of the four domains to identify relevant papers that explored outcomes of child mortality in relation to specified contributory factors. We used principles of structured narrative review, which, while incorporating a systematic literature search, does not apply the same stringent inclusion and exclusion criteria as a full systematic review. This encompasses a broader review of the literature, but is not intended to be comprehensive, and does not attempt to catalogue the quality of each paper.[6, 7] Common themes were identified through perusal of abstracts, and key papers chosen to illustrate emerging themes. Papers cited are not intended to provide a comprehensive review of all research on factors contributing to child mortality in high-income countries, but rather to illustrate core themes in each of the domains.

Panel 1 Baseline Search Strategy

A. Factors intrinsic to the child

Intrinsic (genetic/biologic) factors to child mortality include gender, ethnicity, gestation and growth characteristics, disability, and behaviour.

Gender

Males have a higher mortality rate throughout infancy, childhood and into old age. 2012 mortality data for England and Wales shows male: female mortality ratios of 1.25 in infancy, 1.23 from 1-14 years, and 2.16 from 15-19 years.[8] This is similar to data from the USA , Australia, and other high-income countries.[9,-11] The reasons for this sex mortality differential are complex and include significant biological, environmental, and behavioural factors.[9, 12] Whilst there is a dearth of research in this area, the persistent mortality differential in both perinatal and childhood mortality across time and culture, in spite of overall improvements in medical care, partly points towards biological causation..[13, 14] Kalben suggests that slower male development (both biological and psychological), genetic influences related to the absence of a second X chromosome, and greater resistance to infection among females, may be contributory factors.[9] In the adolescent years, the mortality differential is primarily

related to external causes. 2012 data for England and Wales shows a ratio of 3.82 for external causes of death in the 15-19 year age group, compared to 1.32 for all other causes combined (Figure 1).[8] This may reflect higher levels of aggression and risk-taking behaviour among adolescent males, although sex differentials in some risk-taking behaviours, such as cigarette, alcohol and illegal drug use are decreasing over time.[9] External causes of death show a greater sex differential at *all* ages throughout childhood which suggests that other biological or social influences may play a part in causation. In suicide, male: female differentials have increased over recent years, particularly in Eastern European countries.[15] Moller-Leimkuhler suggests this may be related to cultural factors such as differing gender role perspectives and health-seeking behaviour patterns in young males.[15]

Figure 1: Male: Female sex differentials in mortality, England and Wales, 2012

Ethnicity/Race

Ethnic and racial differences in child mortality are apparent in both national statistics and epidemiological studies.[16, 17] There is a substantial literature exploring differential health outcomes between different racial groups in the USA.[18, 19] For example, US National Center for Health Statistics data for 2008 reported a greater than threefold difference in infant mortality rates by race and ethnicity. Non-Hispanic Black, Puerto Rican, American Indian and Alaskan Native infants had higher mortality rates, while Mexican, Asian, Pacific Islander, Cuban, Central and South American infants had lower mortality rates, than non-Hispanic White infants.[20] Higher mortality rates are often found in minority ethnic groups, whether these be recent immigrant groups[21], or indigenous populations of colonised countries (Panel 2). However, within this broad finding, there are more subtle variations in both overall rates and the patterns of child mortality. The 2006 Confidential Enquiry into Maternal and Child Health (CEMACH) study, Why Children Die, found that English families of Pakistani and Black African origin had overall mortality rates significantly in excess of those seen in white children, while Indian, Bangladeshi and Black Caribbean children had similar rates to the overall population.[22] The reasons for such differences may include genetic predisposition, as well as the effects of consanguinity, cultural factors, and underlying socio-economic variation.[16]

The relationship between ethnicity/race and socio-economic factors is particularly complex. While there is a general trend for higher child mortality rates and worse socio-economic measures in immigrant and minority ethnic populations, studies in the USA and UK have found similar social-class gradients for perinatal, neonatal, postneonatal, and overall infant mortality among different ethnic groups.[23] Davey Smith argues against simplistic approaches to explain ethnic differences as either biological/genetic or economically based, and suggests instead a complex interaction between racial, socio-economic, cultural and other factors.[23] Children of immigrant families may suffer worse health outcomes because of the effects of socio-economic disadvantage, poorer housing and amenities, disrupted social support networks, and restricted access to healthcare and other services.. There may also be structural factors within receiving countries that influence immigration health outcomes. Bollini and colleagues found substantial differences in perinatal mortality, prematurity and low birthweight, among immigrant women in different European countries and argue that immigration policies may play a significant role in these.[22] They conclude that 'where a definite effort to establish strong integration policies has been made the disadvantage is cancelled or at least attenuated, resulting in a sizeable significant reduction in the gap between native and immigrant women'.

Panel 2: Child mortality in Aboriginal populations

Gestation and growth

The period of time that a baby spends *in utero,* and the first 12 months, are critical to establishing the foundations of a healthy life.[31] The first three years are especially important for a child's brain development. Adverse experiences during this time can have life-long effects on intellectual, emotional, and social functioning.[32-34] Low birth weight (LBW; < 2500grams) and preterm birth (< 37 weeks) are associated with long-term morbidity and increased infant and child mortality.[35-39] There is no specific cut off in relation to either, but a gradient with higher risks the lower the birthweight and gestational age.[40] Compared to normal birthweight, LBW babies have a 2 to 3-fold increased mortality at ages 1-4, 5-9, and 10-14 years, [41] and, globally, prematurity remains the leading cause of death in the first four weeks of life, and second leading cause of death after pneumonia in children under the age of five.[40] In most high-income countries, the incidence of preterm birth has increased, [42] and

whilst survival rates have improved, [43, 44] such infants remain at risk of poor long term outcomes, either as a direct consequence of their prematurity (e.g. cerebral palsy) or secondary to more distal factors (e.g.in-utero nutrition or wider social determinants). [45, 46] Independent of gestation, older maternal age and in particular teenage pregnancy is associated with increased risk for adverse perinatal outcomes and long-term effects on mother and child.[47] The prevalence of teenage births varies widely across high income countries: Australia 16.1 births per 1000 women vs USA 29.4 births per 1,000 women. [48, 49] Whether adverse outcomes can be attributed to biological factors, lifestyle choices (smoking, poor nutrition, alcohol use, poor antenatal attendance, sexually transmitted infection) or social disadvantage remains unclear. [50-52]

Disability

Childhood disability is a significant contributor to child mortality outside the neonatal period. In the 2006 UK confidential inquiry, *Why Children Die*, 307 out of 957 deaths occurred in children with developmental delay or disability, of which 173 had identified congenital abnormalities, and 50 had cerebral palsy.[20] In both groups, many children survived into late childhood or their teenage years. In many cases, the increased mortality associated with disability was related either to recognised life-limiting illness, or to factors directly related to the underlying disability such as an increased susceptibility to respiratory infections. A recent UK-wide data-linkage study found that 60% - 70% of children who died had a pre-existing chronic condition, most commonly neurological conditions throughout childhood, and mental and behavioural conditions in adolescence.[42] A recent UK study of deaths in both adults and children with learning disability found that 42% of deaths assessed were considered premature.[53] Factors contributing to this included delays with diagnosis or treatment, and problems with providing appropriate health and social care in response to changing needs. The extent to which such findings would apply to a specific childhood population with disability, and whether this reflects more systemic failings in healthcare for disabled children in general requires further study.

Behaviour

Behaviours such as smoking, alcohol ingestion, drug use, poor diet and physical inactivity, account for substantial morbidity and mortality throughout life, and simultaneous

engagement in such activities during adolescence further increases morbidity and the risk of premature death. [54-56] Whilst usually initiated during adolescence, the frequency of engagement in such behaviours increases during teenage years into early adulthood. [57, 58] There is an association between early alcohol use and multiple risk behaviours. [59] In the UK, nearly half of adolescents have engaged in binge drinking by 15 years of age, and a third in hazardous drinking by 16 years, with no clear difference in gender predisposition. In contrast, the pattern of other individual risk behaviours varies between males and females, with antisocial and criminal behaviour, cannabis-use and vehicle–related problems more prevalent amongst adolescent males, and teenage smoking, self-harm and physical inactivity more common in adolescent females. [60] In later life, the related sequelae to risk-taking behaviours include rising rates of offending behaviour, conduct disorders, and depression.[61, 62.]

B. Factors in the physical environment

The influence of the physical environment on child deaths is highly interrelated with socio-economic, human behavioural, and intrinsic child characteristics. For example, a motor vehicle death precipitated by driver error may occur in a poorly engineered vehicle, and air pollution may be more toxic in children with respiratory disorders. Geography is also an important correlate of physical environment; population density is associated with higher rates of homicides and motor vehicle crashes; disadvantaged children in urban areas are more likely to live near industrialized zones with high concentrations of polluted air and water, whereas those in rural areas may have more exposure to pesticides.[63-65] Table 2 describes factors in the physical environment related to child mortality.

Table 2: Impact of Physical Environment on Child Mortality

Motor vehicle fatalities are a major cause of injury deaths across all age groups in children in high income countries, and are often cited as the number one cause of deaths in adolescents. There is a male gender predominance and, in the US, Hispanic and Black children and teenagers are at significantly higher risk than whites. [66]Although in recent years there have been encouraging declines in motor vehicle fatalities, there remains substantial

variations between and within countries.[41, 67] Sethi et al have estimated that, if all countries in Europe had the same mortality rates from road traffic injuries as those with the lowest rates, nearly 7900 children's lives could be saved each year.[67] This report emphasizes a number of environmental, social and political measures that have been taken to reduce motor vehicle fatalities; for example, limits on passenger numbers, higher penalties for driving infractions, and graduated licensing policies which have lowered adolescent mortality by improving teenage driving behaviour through requiring more practice hours under adult supervision. Improvements in car engineering have also reduced fatalities: structures better able to withstand forces of collisions; safety devices such as airbags, seatbelts, and infant car seats; and rear cameras to prevent driveway backovers. [68, 69] In early childhood, pedestrian fatalities are more common than driver/passenger fatalities. These fatalities have a strong association with children from lower socio-economic groups, communities with high traffic densities, and areas with higher speed zones. [70, 71] Many child deaths are associated with an inattention to street crossings, and research demonstrates that environmental interventions to improve road design and walking spaces are more likely to be successful than efforts to effect young children's behaviour. [71]

There are many features in the physical environment of the home and neighbourhood that increase the risk of fatalities for children. In almost all of situations, low-income, non-white children are at higher risk of living with and dying from these physical hazards.[72] Both inside and outside the home, modifications to the environment can reduce children's and adolescent's exposure to hazards, as well as lessening the potential adverse impact of such exposure. Firearm and poisoning accidents are important examples where hazard exposure directly interfaces with lethal outcomes (Panel 3).

Panel 3: Means matter: Restricting access to lethal means can prevent deaths

Weather and climate change may be factors in child deaths. A small body of literature documents increases in child hyperthermia deaths during periods of extreme heat, when children are left inside closed cars, or during sports activities.[85, 86] There is little evidence that children are more likely to die in natural disasters; for example, following Hurricane Catrina there was no change in child mortality rates.[87] In contrast, the environmental health

literature is beginning to correlate climate change with concomitant increases in mortality rates.[88, 89] One group of authors hypothesise that climate change will affect child mortality across three areas: anthropogenic changes such as air pollution and altered ultraviolet radiation; thermal extremes and extreme weather; and longer-term ecologic changes that alter food availability, allergy/mycotoxin and disease exposure, and emerging infectious diseases. [90] It is speculated that chemical pollutants may be contributing to a rise in Sudden Infant Death Syndrome (SIDS) and respiratory diseases in high income countries.[91, 92] Lastly, ionizing radiation causes childhood leukemia, as evidenced by increased cancer rates in children following the Hiroshima and Nagasaki atomic bomb explosions and the Chernobyl nuclear accident.[93] A US study examining changes in infant mortality and child cancers in the two years following closures of eight nuclear power plants demonstrated that birth defects, cancer incidence, and mortality declined sharply among infants and children living downwind and within 64 km of each plant.[94]

C. Factors in the social environment

Socio-economic status

Many studies reveal a consistent inverse association between socioeconomic status and childhood mortality in high income countries.[47, 95-100] This inverse association appears to be persistent across time, with some evidence of a steepening of the socioeconomic gradient in recent decades in the United States.[101] Furthermore, the relationship appears to hold regardless of whether socioeconomic status is delineated at an individual level, using measures such as income, social class or parental education, or at a more aggregated level using national or regional data on socioeconomic conditions.[102-105]

Panel 4; Socio-economic gradients in child mortality

Several studies demonstrate an inverse association between socioeconomic status and specific causes of childhood mortality, including cancer as a whole, [108] acute lymphoblastic leukaemia, [109] suicide, [110] homicides, [111, 112] injury and poisoning[113] and motor traffic accidents.[112] The most voluminous literature in this area has demonstrated a marked inverse relationship between socioeconomic status and SIDS, which in turn has informed the

design and implementation of public health policy initiatives aimed at its prevention.[114-116] A further body of work explores the relationship between socioeconomic indicators and death during specific periods of childhood[99, 117-120]. There is conflicting evidence on the period of infancy where socioeconomic deprivation has its greatest effect on mortality rates. Evidence from England suggests that it is the neonatal period, [99] while evidence from the Nordic countries[99] and Belgium[121] suggests that it is the post-neonatal period, although comparisons between studies are complicated by differences in the measures used and empirical approaches applied.

While it is important to recognise the persistent socio-economic gradients that exist in our societies, it is even more important to go beyond this to explore the pathways through which these disparities affect child health outcomes. Inherent within this are strong age and gender biases. Women and children tend to be more profoundly affected by social inequalities.[122] There are fewer resources available to mothers to provide for their children's basic needs; poorer access to antenatal care which may affect the wellbeing of both mother and fetus, as well as result in premature delivery and low birthweight; and lastly poorer nutrition and unsafe living environment for which preventative healthcare plays an important role. Furthermore, risk behaviours, such as parental cigarette smoking, and alcohol and substance misuse tend to be strongly socially determined. There may be cumulative disadvantage where, for example, poverty interacts with the effects of disability, or ethnic minority status, or single parenthood.[123] Throughout childhood and adolescence, poor access to healthcare by those who most need it compounds the problems already affecting these children's chances. As Spencer has argued, 'Practice and service structures must seek to overcome the "inverse care law," which states that those most at risk and most in need of services are the least likely to access them. This is a particularly pressing issue in the United States, where many children of families with low income have limited access to child health services, but it is also a problem in the United Kingdom despite the universal availability of high quality pediatric services.' [122]

Parental and wider social characteristics

In contrast to the copious literature on the impact of socioeconomic inequalities on child mortality, there is very little published on broader aspects of the social environment such as

parental characteristics, parenting behaviours, family structures or social support. The main exceptions to this paucity of literature are in studies on SIDS and on deaths from violence. A number of papers have explored the demographics of families in which SIDS occurs. Alongside a general socio-economic gradient, certain characteristics are frequently reported including young maternal age, higher parity, single parenthood and mental health issues.[123, 124] In addition, parenting behaviours are consistently found to be important contributory factors, including parental smoking, drug and alcohol use, and unsafe infant sleeping practices.[125, 126, 127] In relation to fatal child maltreatment, a number of parental characteristics recur, including young maternal age, low level of maternal education, family size, previous abuse, unemployment, parental mental ill-health and substance misuse, domestic violence, and increased parental stress (Panel 5). [128-129]

Panel 5: Social factors affecting child maltreatment fatalities

Aside from the more obvious cases of filicide, poor parental care may be a significant factor in a wide range of deaths related to but not directly caused by maltreatment.[135] Studies report neglect to be a factor in at least 30-40% of maltreatment deaths, and higher levels of poor parental care, inadequate supervision, and failure to respond to the health needs of a child may be an under-recognised factor in other causes of child death.[135, 139]

Non-fatal maltreatment in a child is, in itself, a recognised risk factor both for later fatal maltreatment, and for other causes of mortality including accidental deaths.[129, 130, 130] A past history of maltreatment, including emotional and sexual abuse, is a recognised finding in many cases of adolescent suicide, as is social isolation and peer victimisation.[140]

D. Factors in service delivery

In the analysis of child mortality, factors in service delivery that impact upon outcome may be divided into those that relate to national policy, to healthcare services, and to the individual practitioner (Figure 2). In addition, factors in the delivery of other welfare services (such as housing, welfare benefits, social care) may also have a substantial impact on child health outcomes.

Figure 2. Schema representing factors in Service Delivery that impact upon a child's health outcome

National Health, Social, and Economic Policy

While there have been significant reductions in child mortality rates in all high-income countries, substantial differences remain between countries. Recent international comparisons of health care systems help generate hypotheses regarding the optimal configuration of services but do not allow precise predictions relating to health outcomes.[141] Factors contributing to child death are highly complex and systematic evaluation should recognise ethnic diversity, GDP health expenditure (GDPHE), 'public' versus 'private' models of finance, and income inequality as well as any structural differences in health policy. The five countries in the Western world with the worst child (0-14 years) mortality rates (USA, 24.4 per 10,000; New Zealand 21.1; Portugal 19.3; Canada 18.8, and the UK, 18.3) are those with the widest inequalities in income.[142-144] At the macro-policy level, politicians should recognise that child mortality is as much a consequence of proper socio-economic planning as of changes in health care systems. Investment in child-centric social policies, statutory health education in national school curricula, and public health initiatives will improve outcomes not only for children but also for adults across the age spectrum.[145, 146]

Healthcare services

Healthcare services have historically been separated into community-based (primary care) and hospital-based (secondary or tertiary care) teams. Child diseases might broadly be divided into acute (e.g meningococcal septicaemia) and chronic diseases (e.g. asthma), and each requires a different although inter-related health system solution.

In acute disease, healthcare amenable mortality is dependent upon universal access to a health care professional with the appropriate training and diagnostic capabilities to triage and treat a child in a time-sensitive fashion. However, across Europe, there is huge variation in 'first contact' models and the relative expertise of practitioners. General Practitioners in the UK have a much lower referral rate to hospital specialists than Primary Care Paediatricians in the US.[147] The analysis of 'first contact models' in those countries with

better child survival outcomes can provide useful insight into different ways of integrating healthcare across community and hospital boundaries.[141, 148]

The management of chronic childhood diseases such as asthma, diabetes, and epilepsy, requires a shift in focus from a hospital-centric model of provision to an integrated system that transcends arbitrary boundaries between primary and secondary care. Much might be lifted from the model of chronic care provision in the elderly with collaborative organisational arrangements between health and social services and supportive financial processes. Again, different models of health services allow comparative lessons to be drawn. The Swedish model of multi-professional health centres with co-located primary care practitioners, paediatricians and other key allied health professionals, is an example of how integrated services may result in improved skills, efficiency and continuity of care for children with long term conditions.[141]

Finally, the configuration of *specialist* services, and the model of care for those services is critical to improving patient outcomes (Table 3)

Table 3: Health service delivery factors contributing to child mortality

Variations in outcomes exist, even in hospitals operating under similar systems,. For example, studies have shown that hospitals offering ostensibly the same level of neonatal care report dramatically different complication rates and outcomes. Part of this variation may represent a failure to implement evidence-based best practices. A study of 12 centres with marked variation in extremely premature infant survival rate (52% to 85%.) demonstrated, despite adjustment for socio-demographic variables, significant differences between centres in antenatal and post-natal approaches to resuscitation and use of steroids. [177] Collaborative quality improvement exercises systematically identify 'best practice' from hospitals with the best outcomes and encourage such practice in all hospitals. An example is the Vermont Oxford Network (Panel 6).

Panel 6: The Vermont Oxford Network of Neonatal Intensive Care

Individual Practice

Failure to recognise the severity of illness in sick children is a persisting theme across primary and secondary care. [34,179, 180] This most often occurs at the point of first contact between the sick child and the health care professional, and may involve a failure to understand the importance of the history, to properly examine the patient, to appropriately interpret physical signs, and make a correct diagnosis.[181, 182]

The introduction of treatment algorithms have been shown to improve the management of critically ill patients in the resuscitation room.[183] In a prospective cohort study of admissions to five tertiary paediatric centres, Carcillo et al identified that early reversal of shock by community physicians through the use of resuscitation protocols was associated with reduced mortality (8.69% vs 15.01%) and functional morbidity (*an improved Paediatric Overall Performance category score between admission and discharge*; 1.24% vs 4.23%) after controlling for severity of illness and trauma status (*categorised into those with trauma – isolated head trauma, multi-trauma with head injury, and multi-trauma without head injury – and those without trauma*).[184]

There is a substantial body of literature on patient safety and adverse incidents, and there is not scope to review it within this paper.[185-187] Although it is widely recognized that adverse events arising from medical error are a serious public health concern, it is difficult to estimate the actual incidence of medical error since design and criteria used in studies vary widely. Not all mistakes in medical management cause measurable harm to patients, and not all harm to patients from medical treatment arises from preventable error.[188] Children, especially the very young, those who are socially disadvantaged, and those with more complex or critical care needs are particularly vulnerable to adverse events.[189-192]

Discussion

Through a structured review of the literature, we have identified a wide range of factors influencing child mortality in high income countries. These can be conceptualised within the four domains of factors intrinsic to the child, the physical environment, the social

environment, and service delivery. In a short review, it is not possible to capture the full scope of factors, their variation with different conditions, and the interactions between them. In attempting to understand and learn from an individual child's death, it is important to move beyond a simple categorisation of the cause of death, to consider the question, 'Why did this child die of this condition at this time?' This leads us to reflect on the complex web of interacting factors in each of these four domains. Even this brief review demonstrates that a purely biological or medical approach to understanding child mortality is inadequate. While biological factors, such as infection play a role in many children's deaths, there are others where social or behavioural (child, carer or professional) factors are far more important. It is also clear that the physical and social environment within which a child is living and growing is as important to their health and wellbeing as are their primary material needs.

While some factors, such as a child's gender, age, ethnicity, genetic make-up, some parental characteristics, and some wider environmental conditions are relatively fixed, others may be amenable to interventions that could prevent future child deaths. This is reflected in the high proportion of children's deaths deemed preventable in many systems of child death review.[22, 193, 194] Consideration of those factors that may be amenable to change is important for a population approach to preventing child deaths and improving child health and well-being. Roberts and Jackson have argued in *The Lancet* that 'Much premature death and suffering can be prevented by tackling its causes. Removal of upstream (distal) causes is often more cost effective than is removal of proximal medical causes, because upstream causes bring about a plethora of downstream sufferings.'[195] Tackling socio-economic gradients, child poverty, and overall service configuration requires creative thinking and long-term political commitment. However, it is these macro factors that are more influential in reducing risk through their effect on more proximal systems, structures and behaviours.

A detailed exploration of the complex mechanisms through which socioeconomic inequalities impact upon childhood mortality is beyond the scope of this paper. However, there is broad recognition that biological processes affecting child health and survival are strongly mediated by their socioeconomic context. There exists an inverse socioeconomic gradient for childhood mortality in high income countries. Because this gradient is seen

across such a wide range of contexts, time periods and study designs, the effects of low socioeconomic status are unlikely to be mediated simply through a few recognised biological, behavioural and environmental factors, such as low birthweight, parental smoking, or exposure to infection. It is much more likely that relative poverty itself has wide-ranging effects on health exerted through mechanisms that are still not well understood. Research, therefore, should focus on tackling both the underlying social inequalities that contribute to these disparities, and on their social determinants i.e. those pathways through which social inequalities influence outcome, and particularly those components of a pathway that are amenable to intervention.

Thus, for example, improvements to the physical environment in which children in low-income neighbourhoods are living may yield benefits in reduction of hazard exposures, and improvements in health and wellbeing, even though the underlying socio-economic disparity has not changed. Similarly, changes to local health service configuration to improve access by indigenous populations to preventive care may reduce risk, and targeted intervention for vulnerable parents may enable them to respond more appropriately to their children's needs. In all these circumstances, it is important to identify those interventions for which there is evidence of efficacy and cost-effectiveness.

Children, by their nature, are dependent on others, particularly their parents, to mediate many of the external influences that impact on their health. However, parents who themselves have grown up with disadvantage or are compromised by the choices they have made, for example substance misuse, may not be able to offer adequate and safe parenting, and in some cases will pose a direct risk to their children. Intergenerational cycles can result in cumulative disadvantage and outcomes for these children are likely to be poor where parenting incapacity remains unidentified or untreated. [130, 133] This highlights the need for coordination between child and adult services to deliver an holistic approach to identification of concerns, quality assessment, and information sharing, and then implementation of effective early intervention strategies, with a focus on improved outcomes for the child and family.

Recommendations

Current reflections on avoidable deaths in childhood utilise high-level metrics derived from national offices of vital statistics. Deaths due to 'communicable diseases' are often stated as being 'avoidable' whilst in clinical reality the situation is much more complex. This review of children's deaths in high income countries has indicated a wide range of factors in each of the four domains. Within each of these, action to tackle the underlying causes of mortality is required at a number of levels, including high-level policy, public health, health provider organisations and those commissioning their services, and individual practitioners. It is also important to recognise the crucial role that parents and carers play in the health of their children, and steps that individuals and the wider community can take to improve outcomes.

In Table 4, we suggest some strategies that could be adopted to reduce child mortality, building on the learning from this review. These are based on our review of the literature on risk factors, and are intended as examples, rather than validated or comprehensive strategies. Within each of these domains there are multiple specific interventions that already have a strong evidence base of effectiveness, as well as others which need further research to establish their potential benefit. In designing and implementing preventive strategies, the health community needs to take account of the patterns and burden of disease in the child population; an understanding of modifiable factors contributing to mortality and morbidity; and the efficacy, cost, and acceptability of any preventive intervention.

In addition, there are further high-level considerations, which could contribute to lowering child mortality in high-income countries:

- Governments should agree a common dataset of child mortality indicators that recognises the multi-agency reality of how services are delivered across the patient pathway. Such an initiative would allow a standardised approach to the assessment of modifiable factors contributing to unplanned acute hospital admissions, and the provision of care packages to children with chronic conditions along national guidelines.

- System design should be modelled on current and future child and public health scenarios; namely, an increasing population of children with life-long chronic disorders, complex disability, and obesity. A whole-system approach is required that integrates health care, public health and social welfare, and shifts delivery of services from a hospital- to a community-centric model of care.
- Governments should recognise that child survival and health outcomes across society are linked to socio-economic policies that reduce inequality as much as they are to a country's GDP and systems of health care delivery.

Table 4: Potential interventions to tackle underlying contributory factors contributing to child mortality

Conclusion

Children are among the most vulnerable members of our society. This vulnerability may be further increased by intrinsic factors such as a genetic predispositions or disability, and by extrinsic factors in their physical or social environment, and in the care provided to them. On-going disparities in child mortality between and within countries emphasise not only our reluctance to truly engage with the deep social inequalities inherent in our societies, but also a failure to look beyond simple descriptions of the problem to understand the complex pathways that ultimately lead to poor outcomes for children.

In this paper, we have reviewed some of the literature on different factors contributing to child mortality in high income countries. We provide a framework for considering the role of different factors, based on an understanding of the ecological world of the child. Interventions to reduce preventable child mortality need to take place at a number of different levels, informed by a clear understanding of the interacting risks. As has previously been emphasised,[195] a solution-focused approach will identify interventions of proven efficacy that tackle some of the underlying causes. These have the potential, not only to reduce cause-specific mortality, but to bring much wider benefits to overall child health and well-being.

Author Contributions

All authors contributed to gathering and interpreting data for this paper and to the writing of initial drafts. All authors have seen and approved the final submission.

Conflicts of Interest

Dr Sidebotham runs the Warwick advanced course in the management of unexpected child death. He has received grant money from the Department for Education for research into child death review and the development of training materials on child death review.
Dr Fraser is on the faculty of the Warwick advanced course in the management of unexpected child death.
Theresa Covington is the Director of the US National Center for the Review and Prevention of Child Deaths.

None of the authors have any other conflicts of interest.

Funding

No external funding was received for any of the work in this paper.

Acknowledgments

We are extremely grateful to Samantha Johnson, Academic Librarian, at the University of Warwick, for assisting with the literature searches for this paper.

Key Messages

- Simple categorisations of causes of death by national offices of vital statistics fail to explain 'why did this child die of this condition at this time?'. A purely biological or medical approach to understanding childhood mortality does not reflect the complexity of interacting risks that are best conceptualised within 4 domains: intrinsic child factors, the physical environment, the social environment, and service delivery factors.

- Although factors such as gender, age, ethnicity, inherent genetic make-up, and parental characteristics are relatively fixed, many environmental, social, and health service factors are amenable to interventions that may reduce future child deaths. Analysis of different 'first contact' and 'integrated care' models in countries with better survival outcomes may provide insight into improving health care services across community and hospital boundaries.

- Relative poverty has wide ranging effects on health and there is a persisting inverse association between socio-economic status and childhood mortality in high income countries. At a macro-policy level, child mortality is as much a consequence of proper socio-economic planning as of changes in health care systems alone. Within each of the 4 domains, actions are required at a number of levels including high level policy, public health, health provider organisation, those commissioning their services, as well as individual practitioners.

References

1. Fraser J, Sidebotham P, Covington T, Frederick J. Formal Child Death Review processes: shedding light on children's mortality in high income countries? Lancet. In press.
2. Sidebotham P, Fraser J, Fleming P, Ward-Platt M, Hain R. Child Death Review Series II: Patterns of child death in England and Wales. Lancet. In press.
3. Bronfenbrenner U. "Developmental Research, Public Policy and the Ecology of Childhood". Child Development. 1974; 45: 1-5.
4. Bronfenbrenner U, Evans G. "Developmental science in the 21st century: emerging questions, theoretical models, research designs and empirical findings.". Social development. 2000; **9**: 115-25.
5. Sidebotham P, Fox J, Horwath J, Powell C, Perwez S. Preventing Childhood Deaths: An Observational Study of Child Death Overview Panels in England. London: Department for Children, Schools and Families; 2008.
6. Marriott C, Hamilton-Giachritsis C, Harrop C. Factors Promoting Resilience Following Childhood Sexual Abuse: A Structured, Narrative Review of the Literature. Child Abuse Review. 2013: n/a-n/a.
7. Green BN, Johnson CD, Adams A. Writing narrative literature reviews for peer-reviewed journals: secrets of the trade. Journal of Chiropractic Medicine. 2006; 5(3): 101-17.
8. Office for National Statistics. Mortality Statistics: Deaths registered in England and Wales (Series DR), 2012. London: Office for National Statistics; 2013.
9. Kalben BB. Why Men Die Younger. North American Actuarial Journal. 2000; 4(4): 83-111.
10. Patton GC, Coffey C, Sawyer SM, Viner RM, Haller DM, Bose K, et al. Global patterns of mortality in young people: a systematic analysis of population health data. Lancet. 2009; 374(9693): 881-92.
11. Draper G, Turrell G, Oldenburg B. Health inequalities in Australia: Mortality. Health Inequalities Monitoring Series No.1. AIHW Cat. No. PHE 55. Canberra: Queensland University of Technology and the Australian Institute of Health and Welfare. 2004.
12. Tickle L. The Sex Differential in Mortality Rates and Underlying Factors. Sydney: Macquarie University; 1997
13. Stevenson DK, Verter J, Fanaroff AA, Oh W, Ehrenkranz RA, Shankaran S, et al. Sex differences in outcomes of very low birthweight infants: the newborn male disadvantage. Arch Dis Child Fetal Neonatal Ed. 2000; 83(3): F182-5.
14. Kent AL, Wright IM, Abdel-Latif ME. Mortality and adverse neurologic outcomes are greater in preterm male infants. Pediatrics. 2012; 129(1): 124-31.
15. Moller-Leimkuhler AM. The gender gap in suicide and premature death or: why are men so vulnerable? European archives of psychiatry and clinical neuroscience. 2003; 253(1): 1-8.
16. Alio AP, Richman AR, Clayton HB, Jeffers DF, Wathington DJ, Salihu HM. An ecological approach to understanding black-white disparities in perinatal mortality. Matern Child Health J. 2010; **14**(4): 557-66

17. Anachebe NF. Racial and ethnic disparities in infant and maternal mortality. Ethnicity & disease. 2006; **16**(2 Suppl 3): S3-71-6.
18. Hessol NA, Fuentes-Afflick E. Ethnic Differences in Neonatal and Postneonatal Mortality. Pediatrics. 2005; **115**(1): e44-e51
19. Loggins S, Andrade FC. Despite an Overall Decline in U.S. Infant Mortality Rates, the Black/White Disparity Persists: Recent Trends and Future Projections. Journal of community health. 2013.
20. Macdorman MF, Mathews TJ. Recent trends in infant mortality in the United States. NCHS data brief. 2008; (9): 1-8.
21. Bollini P, Pampallona S, Wanner P, Kupelnick B. Pregnancy outcome of migrant women and integration policy: A systematic review of the international literature. Social Science & Medicine. 2009; 68(3): 452-61.
22. Pearson GE. Why Children Die: A Pilot Study 2006; England (North East, South West and West Midlands), Wales and Northern Ireland. London: CEMACH; 2008.
23. Smith GD. Learning to live with complexity: ethnicity, socioeconomic position, and health in Britain and the United States. Am J Public Health. 2000; 90(11): 1694-8.
24. Smylie J, Crengle S, Freemantle J, Taualii M. Indigenous Birth Outcomes in Australia, Canada, New Zealand and the United States - an Overview. The open women's health journal. 2010; (4): 7-17.
25. Freemantle J, McAullay D, Officer K, Anderson I. Australia Indigenous Health-within an international context. Darwin, Australia: Cooperative Research Centre for Aboriginal Health; 2007.
26. Cattaneo A, Cogoy L, Macaluso A, Tamburlini G. Child Health in the European Union. Trieste, Italy: European Union; 2012.
27. Smylie J, Adomako P. Indigenous Children's Health Report: Health Assessment in Action. Toronto: St. Michael's Hospital; 2009.
28. Anderson I, Crengle S, Kamaka ML, Chen TH, Palafox N, Jackson-Pulver L. Indigenous health in Australia, New Zealand, and the Pacific. Lancet. 2006; 367(9524): 1775-85.
29. US Commission on Civil Rights. Broken promises: evaluating the Native American health care system. Washington: U.S. Commission on Civil Rights; 2004.
30. Freemantle J, Heffernan B. Indigenous children: their human rights, mortality, and the MDG s. United Nations Chronicle. 2010; XLVII(2): 35-8.
31. Gilmore JH, Lin W, Prastawa MW, Looney CB, Vetsa YS, Knickmeyer RC, et al. Regional gray matter growth, sexual dimorphism, and cerebral asymmetry in the neonatal brain. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2007; 27(6): 1255-60.
32. Urban Child Institute. Prematurity and Low Birthweight. Memphis, Tennessee: Urban Child Institute; 2012
33. Winter P. Neuroscience and Early Childhood Development: summary of selected literature and key messages for parenting. Victoria, Australia: Ministerial Council for Education, Early Childhood Development and Youth Affairs 2010.

34. Shonkoff JP, Garner AS, Committee on Psychosocial Aspects of C, Family H, Committee on Early Childhood A, Dependent C, et al. The lifelong effects of early childhood adversity and toxic stress. Pediatrics. 2012; 129(1): e232-46.
35. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics. 2001; 107(1): E1.
36. Stein RE, Siegel MJ, Bauman LJ. Are children of moderately low birth weight at increased risk for poor health? A new look at an old question. Pediatrics. 2006; 118(1): 217-23.
37. Zwicker JG, Harris SR. Quality of life of formerly preterm and very low birth weight infants from preschool age to adulthood: a systematic review. Pediatrics. 2008; 121(2): e366-76.
38. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ. 2012; **345**: e7976.
39. Morse SB, Zheng H, Tang Y, Roth J. Early school-age outcomes of late preterm infants. Pediatrics. 2009; **123**(4): e622-9.
40. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. The Lancet. **371**(9608): 261-9.
41. Hardelid P, Dattani N, Davey J, Pribramska I, Gilbert R. Child Health Reviews UK: Overview of child deaths in the four UK countries. London: Royal College of Paediatrics and Child Health; 2013.
42. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The Lancet. **371**(9606): 75-84.
43. Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, et al. Trends in neonatal morbidity and mortality for very low birthweight infants. American Journal of Obstetrics and Gynecology. 2007; 196(2): 147.e1-.e8.
44. Stoelhorst GMSJ, Rijken M, Martens SE, Brand R, den Ouden AL, Wit J-M, et al. Changes in Neonatology: Comparison of Two Cohorts of Very Preterm Infants (Gestational Age <32 Weeks): The Project on Preterm and Small for Gestational Age Infants 1983 and The Leiden Follow-Up Project on Prematurity 1996-1997. Pediatrics. 2005; **115**(2): 396-405.
45. Smith LK, Draper ES, Manktelow BN, Field DJ. Socioeconomic inequalities in survival and provision of neonatal care: population based study of very preterm infants.[Erratum appears in BMJ. 2009;339:b5196]. BMJ. 2009; 339: b4702.
46. Smith LK, Manktelow BN, Draper ES, Springett A, Field DJ. Nature of socioeconomic inequalities in neonatal mortality: population based study. BMJ. 2010; 341: c6654.
47. Social Exclusion Unit. Teenage Pregnancy. London: Stationery Office, 1999
48. Australian Bureau of Statistics Births, Australia, 2012 Cat Num 3301.0
49. Hamilton, B. E., Martin, J. A., & Ventura, S. J.(2013). Births: Preliminary data for 2012. Hyattsville, MD: National Center for Health Statistics.
50. van der Klis KA, Westenberg L, Chan A, et al. Teenage pregnancy trends, characteristics and outcomes in South Australia and Australia. Aust N Z J Public Health 2002;26:125–31

51. Raatikainen K, Heiskanen N., Verkasalo PK, Heinonen S. Good outcome of teenage pregnancies in high-quality maternity care. European Journal of Public Health. 2006; Vol. 16, No. 2, 157–161.
52. Stevens-Simon C, Beach RK, McGregor JA. Does incomplete growth and development predispose teenagers to preterm delivery? A template for research. J Perinatol 2002; 22:315–23.
53. Heslop P, Blair P, Fleming P, Hoghton M, Marriott A, Russ L. Confidential Inquiry into premature deaths of people with learning disabilities (CIPOLD) Final report. Bristol: Norah Fry Research Centre.; 2013.
54. World Health Organisation. Geneva: World Health Organisatiomn; 2002. The World Health Report 2002; reducing risks, promoting healthy life.
55. Gore F, Bloem P, Patton G, et al. Global burden of disease in young people aged 10-24 years: a systematic analysis. Lancet. 2011; 377:2093-102.
56. Biglan A, Brennan P, Foster S et al. Helping adolescents at risk- prevention of multiple problem behaviours. London: The Guildford Press; 2004.
57. Mason W, Hitch J, Kosterman R et al. Growth in adolescent delinquency and alcohol use in relation to young adult crime, alcohol use disorders, and risky sex: a comparison of youth from low-versus middle income backgrounds. J Child Psychol Psychiatry. 2010; 51(12): 1377-85.
58. Pitkanen T, Lyra A-L, Pulkkinen L. Age of onset of drinking and the use of alcohol in adulthood: a follow-up study from 8-42 for females and males. Addiction. 2005; 100: 652-61.
59. DuRant R, Smith J, Kreiter S et al. The relationship between early age of onset of initial substance use and engaging in multiple health risk beaviours among young adoscents. Arch Pediatr Adolesc Med. 1999; 153(3): 286-91.
60. G.J. MacArthur, M.C. Smith, R. Melotti, J. Heron, J. Macleod, M. Hickman, R.R. Kipping, R. Campbell, G. Lewis 2014 Patterns of alcohol use and multiple risk behaviour by gender during early and late adolescence: the ALSPAC cohort. Journal of Public Health | Vol. 34, No. S1, pp. i20–i30
61. Smith D. Youth Crime and Conduct Disorders: Trends, Patterns, and Causal Explanations. In: Rutter M, Smith D, editors. Psychosocial Disorders in Young People Time Trends and Their Causes. New York: John Wiley and Sons; 1995. p. 389-489.
62. Culbertson FM. Depression and gender. An international review. The American psychologist. 1997; **52**(1): 25-31.
63. Kennedy HG, Iveson RC, Hill O. Violence, homicide and suicide: strong correlation and wide variation across districts. The British journal of psychiatry : the journal of mental science. 1999; **175**: 462-6.
64. Ewing R, Schieber RA, Zegeer CV. Urban sprawl as a risk factor in motor vehicle occupant and pedestrian fatalities. Am J Public Health. 2003; **93**(9): 1541-5.
65. Becares L, Shaw R, Nazroo J, Stafford M, Albor C, Atkin K, et al. Ethnic density effects on physical morbidity, mortality, and health behaviors: a systematic review of the literature. Am J Public Health. 2012; **102**(12): e33-66.
66. Baker SP, Braver ER, Chen L, Pantula JF, Massie D. Motor Vehicle Occupant Deaths Among Hispanic and Black Children and Teenagers. Arch Pediatr Adolesc Med. 1998;152(12):1209-1212

67. Sethi D. European report on child injury prevention. Copenhagen: World Health Organization Europe; 2008.
68. Anthikkat P, Page A, Barker R. Risk factors associated with injury and mortality from paediatric low speed vehicle incidents: a systematic review. International journal of pediatrics. 2013; 2013: 841360.
69. Elliott MR, Kallan MJ, Durbin DR, Winston FK. Effectiveness of child safety seats vs seat belts in reducing risk for death in children in passenger vehicle crashes. Arch Pediatr Adolesc Med. 2006; 160(6): 617-21.
70. Rivara FP, Barber M. Demographic Analysis of Childhood Pedestrian Injuries. Pediatrics. 1985; 76 (3): 375 -381.
71. Roberts I, R Norton R, Jackson R, Dunn R. Effect of environmental factors on risk of injury of child pedestrians by motor vehicles: a case-control study. BMJ. 1995; 310: 91-94.
72. Pomerantz WJ, Dowd MD, Buncher CR. Relationship between socioeconomic factors and severe childhood injuries. Journal of urban health : bulletin of the New York Academy of Medicine. 2001; 78(1): 141-51.
73. Richardson C, Erin G, Hemenway D. Homicide, Suicide and Unintentional Firearm Fatality: Comparing the United States with other High Income Countries. 2003. Journal of Trauma-Injury, Infection and Critical Care. Jan 2011; 70 (1): 238-4.
74. Williams CL, Davidson JA, Montgomery I. Impulsive suicidal behavior. Journal of clinical psychology. 1980; **36**(1): 90-4.
75. Miller M, Hemenway D. Guns and suicide in the United States. N Engl J Med. 2008; **359**(10): 989-91.
76. Carrington P. Gender, gun control, suicide and homicide in Canda. Arch. 1999; **1**: 71-5.
77. Goldney RD. Suicide in Australia: some good news. Med J Aust. 2006; **185**(6): 304.
78. Beautrais AL, Fergusson DM, Horwood LJ. Firearms legislation and reductions in firearm-related suicide deaths in New Zealand. The Australian and New Zealand journal of psychiatry. 2006; **40**(3): 253-9.
79. Loftin C, McDowall D, Wiersema B, Cottey TJ. Effects of restrictive licensing of handguns on homicide and suicide in the District of Columbia. N Engl J Med. 1991; **325**(23): 1615-20.
80. Grossman DC, Mueller BA, Riedy C, Dowd MD, Villaveces A, Prodzinski J, et al. Gun storage practices and risk of youth suicide and unintentional firearm injuries. JAMA. 2005; **293**(6): 707-14.
81. Webster DW, Vernick JS, Zeoli AM, Manganello JA. Association between youth-focused firearm laws and youth suicides. JAMA. 2004; **292**(5): 594-601.
82. Walton WW. An evaluation of the Poison Prevention Packaging Act. Pediatrics. 1982; **69**(3): 363-70.
83. Sibert JR, Craft AW, Jackson RH. Child-resistant packaging and accidental child poisoning. Lancet. 1977; **2**(8032): 289-90.
84. Tenenbein M. Unit-dose packaging of iron supplements and reduction of iron poisoning in young children. Arch Pediatr Adolesc Med. 2005; **159**(6): 557-60.
85. Grundstein A, Null J, Meentemeyer V. Weather, geography, and vehicle-related hyperthermia in children. Geographical review. 2011; **101**(4): 353-70.

86. Hoshi A, Inaba Y. Meteorological conditions and sports deaths at school in Japan, 1993-1998. Int J Biometeorol. 2005; **49**(4): 224-31.
87. Kanter RK. Child mortality after Hurricane Katrina. Disaster medicine and public health preparedness. 2010; **4**(1): 62-5.
88. Knowlton K, Rotkin-Ellman M, Geballe L, Max W, Solomon GM. Six climate change-related events in the United States accounted for about $14 billion in lost lives and health costs. Health Aff (Millwood). 2011; **30**(11): 2167-76.
89. Diaz J, Linares C, Garcia-Herrera R, Lopez C, Trigo R. Impact of temperature and air pollution on the mortality of children in Madrid. Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine. 2004; **46**(8): 768-74.
90. Bunyavanich S, Landrigan CP, McMichael AJ, Epstein PR. The impact of climate change on child health. Ambulatory pediatrics : the official journal of the Ambulatory Pediatric Association. 2003; **3**(1): 44-52.
91. Kaiser R, Romieu I, Medina S, Schwartz J, Krzyzanowski M, Kunzli N. Air pollution attributable postneonatal infant mortality in U.S. metropolitan areas: a risk assessment study. Environmental health : a global access science source. 2004; **3**(1): 4.
92. Woodruff T, Parker J, Schoendorf K. Fine particulate matter: air pollution and selected causes of postneonatal infant mortality in California. Environmental Health Perspectives. 2004; **112**(14): 1365-71
93. Wild CP, Kleinjans J. Children and increased susceptibility to environmental carcinogens: evidence or empathy? Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2003; **12**(12): 1389-94.
94. Mangano JJ, Gould JM, Sternglass EJ, Sherman JD, Brown J, McDonnell W. Infant death and childhood cancer reductions after nuclear plant closings in the United States. Arch Environ Health. 2002; **57**(1): 23-31.
95. Blakely T, Atkinson J, Kiro C, Blaiklock A, D'Souza A. Child mortality, socioeconomic position, and one-parent families: independent associations and variation by age and cause of death. International Journal of Epidemiology. 2003; **32**(3): 410-8.
96. Freemantle N, Wood J, Griffin C, Gill P, Calvert MJ, Shankar A, et al. What factors predict differences in infant and perinatal mortality in primary care trusts in England? A prognostic model. BMJ. 2009; **339**: b2892.
97. Gakidou E, Cowling K, Lozano R, Murray CJL. Increased educational attainment and its effect on child mortality in 175 countries between 1970 and 2009: a systematic analysis. Lancet. 2010; **376**(9745): 959-74.
98. Pickett KE, Wilkinson RG. Child wellbeing and income inequality in rich societies: ecological cross sectional study. BMJ. 2007; 335(7629): 1080.
99. Petrou S, Kupek E, Hockley C, Goldacre M. Social class inequalities in childhood mortality and morbidity in an English population. Paediatric and Perinatal Epidemiology. 2006; 20(1): 14-23.
100. Arntzen A, Nybo Andersen AM. Social determinants for infant mortality in the Nordic countries, 1980-2001. Scandinavian Journal of Public Health. 2004; 32(5): 381-9.

101. Singh GK, Kogan MD. Widening socioeconomic disparities in US childhood mortality, 1969 2000. American Journal of Public Health. 2007; 97(9): 1658-65.
102. Sparks PJ, McLaughlin DK, Stokes CS. Differential neonatal and postneonatal infant mortality rates across US counties: the role of socioeconomic conditions and rurality. Journal of Rural Health. 2009; 25(4): 332-41.
103. Regidor E, Pascual C, Martinez D, Calle ME, Ortega P, Astasio P. The role of political and welfare state characteristics in infant mortality: a comparative study in wealthy countries since the late 19th century. International Journal of Epidemiology. 2011; 40(5): 1187-95.
104 Dominguez-Berjon MF, Benach J, Garcia-Arcal MD, Borrell C. Infant and perinatal mortality in Spain 1981-1991: interprovincial variations in Autonomous Communities with extreme economic levels. European Journal of Epidemiology. 1999; 15(8): 723-9.
105. Finch BK. Early Origins of the Gradient: The Relationship between Socioeconomic Status and Infant Mortality in the United States. Demography. 2003; 40(4): 675-99.
106. Rodwin VG, Neuberg LG. Infant mortality and income in 4 world cities: New York, London, Paris, and Tokyo. Am J Public Health. 2005; **95**(1): 86-90.
107. Spencer N. The effect of income inequality and macro-level social policy on infant mortality and low birthweight in developed countries - a preliminary systematic review. Child Care Health and Development. 2004; **30**(6): 699-709.87.
108. Kong KA, Khang Y-H, Cha ES, Moon EK, Lee YH, Lee WJ. Childhood cancer mortality and socioeconomic position in South Korea: a national population-based birth cohort study. Cancer Causes & Control. 2010; **21**(10): 1559-67.
109. Lightfoot TJ, Johnston WT, Simpson J, Smith AG, Ansell P, Crouch S, et al. Survival from childhood acute lymphoblastic leukaemia: the impact of social inequality in the United Kingdom. European Journal of Cancer. 2012; **48**(2): 263-9.
110. Agerbo E, Nordentoft M, Mortensen PB. Suicide in young people - familial, psychiatric, and socioeconomic risk factors - nested case-control study. Ugeskrift for Laeger. 2002; 164(49): 5786-90.
111. Birken CS, Parkin PC, To T, Wilkins R, Macarthur C. Neighborhood Socioeconomic Status and Homicides Among Children in Urban Canada. Pediatrics. 2009; 123(5): E815-E9.
112. Hjern A, Bremberg S. Social aetiology of violent deaths in Swedish children and youth. Journal of Epidemiology & Community Health. 2002; 56(9): 688-92.
113. Edwards P, Roberts I, Green J, Lutchmun S. Deaths from injury in children and employment status in family: analysis of trends in class specific death rates. BMJ. 2006; 333(7559): 119.
114. Spencer N, Logan S. Sudden unexpected death in infancy and socioeconomic status: a systematic review. Journal of Epidemiology and Community Health. 2004; 58(5): 366-73.
115. Pickett KE, Luo Y, Lauderdale DS. Widening social inequalities in risk for sudden infant death syndrome. American Journal of Public Health. 2005; 95(11): 1976-81.
116. Wood AM, Pasupathy D, Pell JP, Fleming M, Smith GCS. Trends in socioeconomic inequalities in risk of sudden infant death syndrome, other causes of

infant mortality, and stillbirth in Scotland: population based study. BMJ. 2012; 344: e1552.
117. Calling S, Li X, Sundquist J, Sundquist K. Socioeconomic inequalities and infant mortality of 46,470 preterm infants born in Sweden between 1992 and 2006. Paediatric and Perinatal Epidemiology. 2011; **25**(4): 357-65.
118. Guildea ZE, Fone DL, Dunstan FD, Sibert JR, Cartlidge PH. Social deprivation and the causes of stillbirth and infant mortality. Archives of Disease in Childhood. 2001; 84(4): 307-10.
119. Arntzen A, Samuelsen SO, Daltveit AK, Stoltenberg C. Post-neonatal mortality in Norway 1969-95: a cause-specific analysis. International Journal of Epidemiology. 2006; 35(4): 1083-9.
120. Son J-Y, Lee J-T. The effect of sociodemographic factors on infant mortality according to cause of death: a birth cohort in Seoul, Korea, 1999-2003. International Journal of Public Health. 2011; 56(1): 7-13.
121. Cammu H, Martens G, Van Maele G, Amy J-J. The higher the educational level of the first-time mother, the lower the fetal and post-neonatal but not the neonatal mortality in Belgium (Flanders). European Journal of Obstetrics, Gynecology, & Reproductive Biology. 2010; 148(1): 13-6.
122. Spencer N. Social, Economic, and Political Determinants of Child Health. Pediatrics. 2003; **112**(Supplement 3): 704-6.
123. Bauman LJ, Silver EJ, Stein REK. Cumulative Social Disadvantage and Child Health. Pediatrics. 2006; **117**(4): 1321-8.
124. Blair PS, Sidebotham P, Berry PJ, Evans M, Fleming PJ. Major epidemiological changes in sudden infant death syndrome: a 20-year population-based study in the UK. Lancet. 2006; **367**(9507): 314-9.
125. Fleming P, Blair P, Bacon C, Berry P. Sudden unexpected deaths in infancy. The CESDI SUDI studies 1993-1996. London: The Stationery Office; 2000.
126. Blair PS, Sidebotham P, Evason-Coombe C, Edmonds M, Heckstall-Smith EM, Fleming P. Hazardous cosleeping environments and risk factors amenable to change: case-control study of SIDS in south west England. BMJ. 2009; **339**: b3666.
127. Vennemann MM, Findeisen M, Butterfass-Bahloul T, Jorch G, Brinkmann B, Kopcke W, et al. Modifiable risk factors for SIDS in Germany: results of GeSID. Acta Paediatr. 2005; **94**(6): 655-60.
128. Berger RP, Fromkin JB, Stutz H, Makoroff K, Scribano PV, Feldman K, et al. Abusive head trauma during a time of increased unemployment: a multicenter analysis. Pediatrics. 2011; **128**(4): 637-43.
129. Stiffman MN, Schnitzer PG, Adam P, Kruse RL, Ewigman BG. Household composition and risk of fatal child maltreatment. Pediatrics. 2002; **109**(4): 615-21.
130. Cavanagh K, Dobash RE, Dobash RP. Men who murder children inside and outside the family. British Journal of Social Work. 2005; **35**(5): 667-88.
131. Schnitzer PG, Ewigman BG. Household composition and fatal unintentional injuries related to child maltreatment. J Nurs Scholarsh. 2008; **40**(1): 91-7.
132. Strine TW, Chapman DP, Balluz L, Mokdad AH. Health-related quality of life and health behaviors by social and emotional support. Their relevance to psychiatry and medicine. Social Psychiatry & Psychiatric Epidemiology. 2008; **43**(2): 151-9.

133. Jonson-Reid M, Chance T, Drake B. Risk of death among children reported for nonfatal maltreatment.[Erratum appears in Child Maltreat. 2007 May;12(2):199]. Child Maltreat. 2007; **12**(1): 86-95.
134. Brandon M, Bailey S, Belderson P, Gardner R, Sidebotham P, Dodsworth J, et al. Understanding Serious Case Reviews and their Impact. A Biennial Analysis of Serious Case Reviews 2005-07. London: Department for Children, Schools and Families; 2009.
135. Sidebotham P, Bailey S, Belderson P, Brandon M. Fatal child maltreatment in England, 2005-2009. Child Abuse & Neglect. 2011; **35**(4): 299-306.
136. Bourget D, Gagne P. Maternal filicide in Quebec. J Am Acad Psychiatry Law. 2002; **30**(3): 345-51.
137. Bourget D, Gagne P. Paternal filicide in Quebec. Journal of the American Academy of Psychiatry & the Law. 2005; **33**(3): 354-60.
138. Nielssen OB, Large MM, Westmore BD, Lackersteen SM. Child homicide in New South Wales from 1991 to 2005. Med J Aust. 2009; **190**(1): 7-11.
139. Berkowitz CD. Fatal child neglect. Adv Pediatr. 2001; **48**: 331-61.
140. King CA, Merchant CR. Social and interpersonal factors relating to adolescent suicidality: a review of the literature. Arch. 2008; **12**(3): 181-96.
141. Wolfe I, Thompson M, Gill P, Tamburlini G, Blair M, van den Bruel A, et al. Health services for children in western Europe. Lancet. 2013; **381**(9873): 1224-34.
142. Pritchard C, Williams R. Poverty and child (0-14 years) mortality in the USA and other Western countries as an indicator of "how well a country meets the needs of its children" (UNICEF). International journal of adolescent medicine and health. 2011; **23**(3): 251-5.
143. Collison D, Dey C, Hannah G, Stevenson L. Income inequality and child mortality in wealthy nations. J Public Health (Oxf). 2007; **29**(2): 114-7.
144. Pritchard C, Wallace MS. Comparing the USA, UK and 17 Western countries' efficiency and effectiveness in reducing mortality. JRSM short reports. 2011; **2**(7): 60.
145. WHO Commission on Social Determinants of Health., World Health Organization. Closing the gap in a generation : health equity through action on the social determinants of health : Commission on Social Determinants of Health final report. Geneva, Switzerland: World Health Organization, Commission on Social Determinants of Health; 2008.
146. Formby E et al.. Personal, Social, Health, and Economic (PSHE) education: A mapping study of the prevalent models of delivery and their effectiveness. 2011. DE.
147. Forrest CB, Majeed A, Weiner JP, Carroll K, Bindman AB. Referral of children to specialists in the United States and the United kingdom. Arch Pediatr Adolesc Med. 2003; **157**(3): 279-85.
148. Wolfe I, Cass H, Thompson MJ, Craft A, Peile E, Wiegersma PA, et al. Improving child health services in the UK: insights from Europe and their implications for the NHS reforms. BMJ. 2011; **342**: d1277.
149. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Annals of internal medicine. 2002; **137**(6): 511-20.

150. Chowdhury MM, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. The British journal of surgery. 2007; **94**(2): 145-61.
151. Stark J, Gallivan S, Lovegrove J, Hamilton JR, Monro JL, Pollock JC, et al. Mortality rates after surgery for congenital heart defects in children and surgeons' performance. Lancet. 2000; **355**(9208): 1004-7.
152. Hornik CP, He X, Jacobs JP, Li JS, Jaquiss RD, Jacobs ML, et al. Relative impact of surgeon and center volume on early mortality after the Norwood operation. Ann Thorac Surg. 2012; **93**(6): 1992-7.
153. Binder S, Hill K, Meinzen-Derr J, Greenberg JM, Narendran V. Increasing VLBW deliveries at subspecialty perinatal centers via perinatal outreach. Pediatrics. 2011; **127**(3): 487-93.
154. Heller G, Schnell R, Richardson DK, Misselwitz B, Schmidt S. [Assessing the impact of delivery unit size on neonatal survival: estimation of potentially avoidable deaths in Hessen, Germany, 1990-2000]. Dtsch Med Wochenschr. 2003; **128**(13): 657-62.
155. Lockwood CJ LJE. American Academy of Pediatrics, American College of Obstetrics and Gynecology Guidelines for perinatal care. Elk Grove Village, Il.: American Academy of Pediatrics; 2008.
156. Ewart H. The relation between volume and outcome in paediatric cardiac surgery. A literature review for the National Specialised Commissioning Group. Oxford: Public Health Research Unit.; 2009.
157. Pasquali SK, Li JS, Burstein DS, Sheng S, O'Brien SM, Jacobs ML, et al. Association of center volume with mortality and complications in pediatric heart surgery. Pediatrics. 2012; **129**(2): e370-6.
158. Pollack MM, Alexander SR, Clarke N, Ruttimann UE, Tesselaar HM, Bachulis AC. Improved outcomes from tertiary center pediatric intensive care: a statewide comparison of tertiary and nontertiary care facilities. Critical care medicine. 1991; **19**(2): 150-9.
159. Gemke RJ, Bonsel GJ. Comparative assessment of pediatric intensive care: a national multicenter study. Pediatric Intensive Care Assessment of Outcome (PICASSO) Study Group. Critical care medicine. 1995; **23**(2): 238-45.
160. Pearson G, Shann F, Barry P, Vyas J, Thomas D, Powell C, et al. Should paediatric intensive care be centralised? Trent versus Victoria. Lancet. 1997; **349**(9060): 1213-7.
161. Potoka DA, Schall LC, Gardner MJ, Stafford PW, Peitzman AB, Ford HR. Impact of pediatric trauma centers on mortality in a statewide system. J Trauma. 2000; **49**(2): 237-45.
162. Edge WE, Kanter RK, Weigle CG, Walsh RF. Reduction of morbidity in interhospital transport by specialized pediatric staff. Critical care medicine. 1994; **22**(7): 1186-91.
163. Orr RA, Felmet KA, Han Y, McCloskey KA, Dragotta MA, Bills DM, et al. Pediatric specialized transport teams are associated with improved outcomes. Pediatrics. 2009; **124**(1): 40-8.
164. Ramnarayan P, Thiru K, Parslow RC, Harrison DA, Draper ES, Rowan KM. Effect of specialist retrieval teams on outcomes in children admitted to paediatric

intensive care units in England and Wales: a retrospective cohort study. Lancet. 2010; **376**(9742): 698-704.
165. NCEPOD. Surgery in children: are we there yet? London: National confidential enquiry into patient outcome and death; 2011.
166. NCEPOD. Trauma: who cares? London: National confidential enquiry into patient outcome and death; 2007.
167. Wallace DJ, Angus DC, Barnato AE, Kramer AA, Kahn JM. Nighttime intensivist staffing and mortality among critically ill patients. N Engl J Med. 2012; **366**(22): 2093-101.
168. Tenner PA, Dibrell H, Taylor RP. Improved survival with hospitalists in a pediatric intensive care unit. Critical care medicine. 2003; **31**(3): 847-52.
169. Numa A, Williams G, Awad J, Duffy B. After-hours admissions are not associated with increased risk-adjusted mortality in pediatric intensive care. Intensive Care Med. 2008; **34**(1): 148-51.
170. Arias Y, Taylor DS, Marcin JP. Association between evening admissions and higher mortality rates in the pediatric intensive care unit. Pediatrics. 2004; **113**(6): e530-4.
171. Peeters B, Jansen NJ, Bollen CW, van Vught AJ, van der Heide D, Albers MJ. Off-hours admission and mortality in two pediatric intensive care units without 24-h in-house senior staff attendance. Intensive Care Med. 2010; **36**(11): 1923-7.
172. Tromp M, Eskes M, Reitsma JB, Erwich JJ, Brouwers HA, Rijninks-van Driel GC, et al. Regional perinatal mortality differences in the Netherlands; care is the question. BMC Public Health. 2009; **9**: 102.
173. Evers AC, Brouwers HA, Hukkelhoven CW, Nikkels PG, Boon J, van Egmond-Linden A, et al. Perinatal mortality and severe morbidity in low and high risk term pregnancies in the Netherlands: prospective cohort study. BMJ. 2010; **341**: c5639.
174. Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GC. Time of birth and risk of neonatal death at term: retrospective cohort study. BMJ. 2010; **341**: c3498.
175. Gijsen R, Hukkelhoven CW, Schipper CM, Ogbu UC, de Bruin-Kooistra M, Westert GP. Effects of hospital delivery during off-hours on perinatal outcome in several subgroups: a retrospective cohort study. BMC Pregnancy Childbirth. 2012; **12**: 92.
176. Vohr BR, Wright LL, Dusick AM, Perritt R, Poole WK, Tyson JE, et al. Center differences and outcomes of extremely low birth weight infants. Pediatrics. 2004; **113**(4): 781-9.
177. Rogowski JA, Staiger DO, Horbar JD. Variations in the quality of care for very-low-birthweight infants: implications for policy. Health Aff (Millwood). 2004; **23**(5): 88-97.
178. Payne NR, Finkelstein MJ, Liu M, Kaempf JW, Sharek PJ, Olsen S. NICU practices and outcomes associated with 9 years of quality improvement collaboratives. Pediatrics. 2010; **125**(3): 437-46.
179. Holden J, O'Donnell S, Brindley J, Miles L. Analysis of 1263 deaths in four general practices. Br J Gen Pract. 1998; **48**(432): 1409-12.
180. Raine JE. An analysis of successful litigation claims in children in England. Arch Dis Child. 2011; **96**(9): 838-40.

181. Harnden A, Mayon-White R, Mant D, Kelly D, Pearson G. Child deaths: confidential enquiry into the role and quality of UK primary care. Br J Gen Pract. 2009; **59**(568): 819-24.
182. Ninis N, Phillips C, Bailey L, Pollock JI, Nadel S, Britto J, et al. The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases. BMJ. 2005; **330**(7506): 1475.
183. Bernhard M, Becker TK, Nowe T, Mohorovicic M, Sikinger M, Brenner T, et al. Introduction of a treatment algorithm can improve the early management of emergency patients in the resuscitation room. Resuscitation. 2007; **73**(3): 362-73.
184. Carcillo JA, Kuch BA, Han YY, Day S, Greenwald BM, McCloskey KA, et al. Mortality and functional morbidity after use of PALS/APLS by community physicians. Pediatrics. 2009; **124**(2): 500-8.
185. Reason JT. Human error. Cambridge England ; New York: Cambridge University Press; 1990.
186. Vincent CA. Analysis of clinical incidents: a window on the system not a search for root causes. Qual Saf Health Care. 2004; **13**(4): 242-3.
187. Vincent CD. Patient safety. 2nd ed. ed. Oxford: Wiley-Blackwell; 2010.
188. Kohn L, Corrigan J, Donaldson ME. To err is human. Washington DC: National Academy Press; 1999.
189. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care. 2008; **17**(3): 216-23.
190. Miller MR, Zhan C. Pediatric patient safety in hospitals: a national picture in 2000. Pediatrics. 2004; **113**(6): 1741-6.
191. Ligi I, Arnaud F, Jouve E, Tardieu S, Sambuc R, Simeoni U. Iatrogenic events in admitted neonates: a prospective cohort study. Lancet. 2008; **371**(9610): 404-10.
192. Agarwal S, Classen D, Larsen G, Tofil NM, Hayes LW, Sullivan JE, et al. Prevalence of adverse events in pediatric intensive care units in the United States. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2010; **11**(5): 568-78.
193. Onwuachi-Saunders C, Forjuoh SN, West P, Brooks C. Child death reviews: a gold mine for injury prevention and control. Inj Prev. 1999; **5**(4): 276-9.
194. Department for Education. Child Death Reviews: Year ending 31 March 2011. London: Department for Education; 2011.
195. Roberts I, Jackson R. Beyond disease burden: towards solution-oriented population health. Lancet. 2013; **381**(9884): 2219-2