Socioeconomic inequalities in survival in neonates
Access to good intensive care blunts the effects of deprivation

In the linked prospective cohort study, Smith and colleagues assessed socioeconomic inequalities in survival and neonatal care provision among very preterm infants. A cohort of 7449 infants born during a 10 year period (1998-2007) at between 22+0 and 32+6 weeks’ gestation were followed up until discharge from neonatal care. What do the findings suggest about equity of neonatal care provision?

Preterm birth is a leading cause of infant mortality worldwide and a substantial cause of childhood disability in survivors. The risks of death are highest in babies born before 33 weeks’ gestation—the very preterm group. Furthermore, both preterm birth and infant mortality are associated with socioeconomic position, with the risks being highest in those from the most deprived socioeconomic groups. As might be expected, the most striking socioeconomic inequalities in neonatal survival are seen from a global perspective, with 98% of neonatal deaths occurring in less developed countries. However, even in high income countries, large overall reductions in infant deaths have not been accompanied by a reduction in socioeconomic inequality in infant mortality. Although the problem of preterm birth remains fairly intractable, greater use of obstetric interventions, such as antenatal steroids, and advances in neonatal care for the very preterm group have led to dramatic increases in survival during the past 30 years. Reductions in neonatal mortality, therefore, depend on access to high quality obstetric and neonatal care.

In England, after a service review in 2003, neonatal units were reorganised into 23 regional neonatal networks, which provided tiered levels of care to facilitate access to such services. However, the effects of this reorganisation have not yet been evaluated. Studies covering the period before this found higher rates of babies from the most deprived group are higher than those for the least deprived group. 1-3

Smith and colleagues’ findings may help to clarify the association between socioeconomic status, neonatal survival, and the equitable provision of neonatal care in the U.K. Mothers from the most deprived areas of the old Trent region of England giving birth in the 10 year period were nearly twice as likely to have a very preterm birth than were mothers from the least deprived areas (incidence rate ratio 1.94, 95% confidence interval 1.62 to 2.32). However, the survival rates of those born very preterm and the provision of neonatal care were not associated with deprivation.

Commentators have warned that interventions to reduce mortality may reduce disparities in health outcomes only if the intervention is highly efficacious and if socially generated barriers do not affect access to care. Neonatal care is efficacious, as the decline in neonatal mortality despite stable or increasing rates of prematurity shows. Smith and colleagues found that access to neonatal intensive care units blunts the effects of deprivation on infant death in very preterm infants; this effect has been shown by others when barriers to care are reduced for traditionally disadvantaged populations in other settings. Efficacious interventions do not always reduce disparities, however. This was shown when surfactant was introduced in the United States, where white infants benefited more than black ones. Achieving equitable outcomes also requires that medical care be equally efficacious across all settings, and that deprivation does not result in reliance on institutions with poorer outcomes, as was reported for New York City.

Clearly further work on quality, equity, and efficiency of neonatal services is essential, but Smith and colleagues reiterate the consistently reported finding that, despite improvements in obstetric and neonatal services, socioeconomic inequalities in preterm birth rates persist. A report on preterm birth from the US Institute of Medicine has reviewed current knowledge on the causes and prevention of these inequalities. Despite the wealth of information on many of the known risk factors, which co-occur particularly in socially disadvantaged women and in women from black and minority ethnic groups, the ways in which they cause preterm birth are poorly understood.

Further progress on preventing preterm birth in general and reducing socioeconomic inequalities in preterm birth is unlikely to occur without a better understanding of the role of socioeconomic factors. Future research should focus on the interplay between the wider determinants of socioeconomic inequalities in health and the biological pathways to parturition. 11

---

The case for population-wide salt reduction gets stronger

A meta-analysis of cohort studies confirms its benefits for preventing stroke and heart disease

Excess intake of salt (sodium chloride) has an important and probably predominant role in the pathogenesis of raised blood pressure. The evidence is indisputable—on average, as salt intake increases, blood pressure increases. Animal studies, migration studies, ecological studies, longitudinal observational studies, clinical trials, and meta-analyses of trials have confirmed this association.1 The importance of this association cannot be overstated—blood pressure is an aetiologically relevant and modifiable cardiovascular risk factor, which has guided policy makers for decades.

Worldwide, raised blood pressure accounts for around 62% of strokes and 49% of coronary heart disease events.2 Large scale trials and meta-analyses of trials have conclusively shown that several treatments that reduce blood pressure prevent stroke and coronary heart disease.3 This compelling evidence has led numerous authoritative bodies to conclude that salt reduction, through its effects on blood pressure, should also prevent stroke and coronary heart disease. Direct evidence to support calls for salt reduction has been limited, however, so the linked meta-analysis of cohort studies by Strazzullo and colleagues is a useful and welcome addition to the medical literature.4

The projected benefits of salt reduction are substantial. Several studies have estimated the societal benefits of population-wide salt reduction. Asaria and colleagues estimated that across 23 countries with a high burden of chronic disease, 850 000 lives would be saved each year from a reduction in salt intake to 5 g a day, the recommended limit set by the World Health Organization.5 In a recent analysis, reducing average sodium intake to the upper limit of recommended intake in the United States (5.8 g a day of salt, equivalent to 100 mmol a day or 2300 mg a day of sodium) should reduce the prevalence of hypertension by 11 million, save $18bn (£10.8bn; €12bn) in healthcare costs, and gain 312 000 quality-adjusted life years.6 Nonetheless, this line of reasoning is indirect. Salt reduction lowers blood pressure (this has been proved), and lowering blood pressure prevents cardiovascular events (so has this).

Evidence of a direct association between salt intake and cardiovascular disease in humans has been sparse, however, owing largely to methodological challenges in conducting appropriate studies. Direct evidence has come from the results of clinical trials and prospective observational studies with cardiovascular disease events as outcomes. To date, three trials conducted in general populations have reported the effects of reduced sodium interventions on such outcomes. Two of these trials tested lifestyle interventions that focused on reducing salt intake,7 8 and one trial tested the effects of reduced sodium salt that is high in potassium.9 In each instance, clinically important cardiovascular disease events were reduced by 21-41% in people who received an intervention to reduce sodium intake (significant reduction in two trials,9 10; non-significant trend in the third).11 Hence, direct evidence from trials, albeit limited, is consistent with indirect evidence on the health benefits of salt reduction.

The most perplexing body of evidence on the health effects of dietary salt intake comes from prospective observational studies that relate estimated salt intake to subsequent stroke and cardiovascular disease. A host of methodological problems plague this literature. Major concerns are random and systematic errors in the measurement of dietary salt intake. Because of large day to day variation in salt consumption, imprecise and inaccurate measurement techniques, and incomplete assessment of dietary intake, results from prospective observational studies have been inconsistent and occasionally paradoxical.

In this setting, the meta-analysis by Strazzullo and colleagues is a useful and welcome addition to the medical literature.1 In their analysis of 13 cohort studies with 19 independent samples, a higher salt intake was associated with an increased risk of stroke, and, probably, cardiovascular disease. Specifically, an 86 mmol/day increase in sodium intake (~5 g a day of salt) was associated with a 23% higher risk of stroke (P=0.007). The association between cardiovascular disease and salt intake was of borderline significance (14% greater
risk of cardiovascular disease, P=0.07). However, in sensitivity analyses that excluded one study with particularly unreliable estimates of sodium intake, the corresponding effect size was 17%, and the association was significant (P=0.02).

The disparate and often poor quality of measurements of dietary salt probably contributed to the significant heterogeneity in the study results seen by Strazzullo and colleagues. The gold standard to assess dietary salt intake is urinary excretion of sodium, as assessed from multiple complete 24 hour urine collections. Yet in only four of the 13 studies were 24 hour urine samples collected, and in none of these studies was more than one collection obtained. More importantly, several studies had evidence of substantial non-systematic under-reporting of salt intake,10–12 and most other studies provided no data on the completeness of dietary assessment.

Policy makers have previously dismissed the results from prospective observational studies in favour of the considerably more robust body of evidence that links salt intake with blood pressure. At a minimum, Strazzullo and colleagues’ analyses should dispel any residual belief that salt reduction might be harmful (a canard resulting from misinterpretation of studies, often with flawed analyses). The case for population-wide salt reduction is now stronger. A reduced intake of salt not only lowers blood pressure but also prevents its major sequelae—stroke and other cardiovascular diseases.

The immediate costs of pandemic influenza to the NHS are easy to imagine, given increased demand across the spectrum of health care—from general practice for milder cases to intensive care for the most sick. The opportunity cost of this is to ration care away from other patients as resources are focused on the care of those with influenza, particularly those with serious complications, and to the creation and delivery of an effective vaccine. From an organisational viewpoint, meeting the needs of people with pandemic flu threatens performance, such as waiting times, in other areas of health care. It also makes clinical decisions about who will be treated when, and who will be left in avoidable pain and discomfort—or possibly to die, even more difficult.

Another consequence of a pandemic is its effect on the economy, and this is the focus of the linked study by Smith and colleagues,1 which uses a computer model to estimate the “economy-wide impact” of pandemic flu in the United Kingdom. This is essentially a cost of illness study that explores the possible financial costs of the illness—derived particularly from absence from work because of illness, fear of illness, and school closure—along with the costs and savings that would result from vaccination. Depending on the assumptions used, and using data from 2004, the authors predict a reduction in gross domestic product (GDP) of between 0.5% and 4.3%, which translates to reductions in UK output of between £8.4bn (€9.4bn; $14bn) and £72.3bn.

These startling figures are a product of assumptions incorporated into the model, and the authors acknowledge that the evidence base for these is highly imperfect. This uncertainty is reflected by the wide range in the estimates. For example, as a pandemic progresses, what would be the level of prophylactic absenteeism from work, as employees fear infection and elect to stay at home rather than mix in a work environment? How many of those who stay at home can work from home, avoiding some of the productivity costs? The likely margins of error for this variable, as well as other clinical and epidemiological variables, are considerable and are accommodated in these model estimates by alternative assumptions. There may also be assumptions in the model that can be affected by NHS staff—for example, those in public health and general practice have a role in, where appropriate, offering reassurance to the public, influencing their perceptions of the risks of illness, and thus affecting the transition point where people chose not to come to work.
Diagnosis of diabetes using the oral glucose tolerance test

May be inaccurate in some ethnic groups, and better tests are needed

The prevalence of type 2 diabetes varies greatly by ethnic group within and across countries. The most reliable data on the prevalence of diabetes are based on two hour plasma glucose values after an oral glucose tolerance test, which is currently the gold standard epidemiological and clinical diagnostic test for diabetes and impaired glucose tolerance. In Newcastle, England, on the basis of clinical evidence and oral glucose tolerance test results, about 20% of British South Asians had diabetes, compared with only 4% of white Europeans, after age adjustment in a sample of 25-74 year olds. Might such observed differences in prevalence, at least in part, be artefacts of the diagnostic method?

In 1965, the World Health Organization expert committee drew attention to the “lack of suitable epidemiological information about glucose tolerance in various populations of various races and cultures in different countries” and highlighted the need for research in different populations. The call was repeated in 1980, with special reference to the oral glucose tolerance test and the dose of glucose, with 75 g being recommended pending further investigations. The International Diabetes Federation in consultation with WHO and the American Diabetes Association (ADA) have raised similar concerns, particularly about the oral glucose tolerance test. With a 75 g dose, a venous plasma glucose value of 11.1 mmol/l or more is indicative of diabetes, as indicated by its association with complications such as retinopathy. A value of 7.8-11.0 mmol/l is indicative of impaired glucose tolerance. Yet these concerns have not been dealt with.

The prevalence of diabetes is increasing worldwide, and accurate testing is more important than ever. The best way to make a diagnosis has been debated for decades, and more guidance is imminent. In some ethnic groups, comparatively low fasting plasma glucose concentrations are seen in people who have two hour postload glucose values that are diagnostic for diabetes.

In the light of these concerns it is vital to know whether the 75 g carbohydrate load is appropriate for all adults, regardless of ethnicity. Glucose tolerance is influenced by several factors—from genetics, to body build (height and weight), to diet and lifestyle. Differences in body composition and skeletal muscle mass are important determinants of postprandial glucose metabolism, and height measurement partly reflects such differences.
An independent inverse association with two hour plasma glucose after the oral glucose tolerance test has been repeatedly shown for height in diverse populations. In a study of the prevalence of type 2 diabetes in white Europeans, African-Caribbeans, and Pakistanis, height almost completely accounted for ethnic differences in two hour plasma glucose in multiple regression models. Pakistanis, in whom the prevalence was the greatest, were markedly shorter (by 2-5 cm) than people in other ethnic groups. The implications of these findings are that a uniform oral glucose load may not accurately assess glucose tolerance across populations, and a high two hour plasma glucose after the oral glucose tolerance test may over-diagnose impaired glucose tolerance in some ethnic groups compared with white populations.

Other factors related to body composition that vary by ethnicity may also be important. Varying the glucose load, as is done in children, or adjusting the results according to ethnicity or height (or both), may improve measures of glucose tolerance. These general observations could have wider implications in explaining inequalities. Impaired fasting glucose is more prevalent in men, whereas impaired glucose tolerance is more prevalent in women. Women are generally shorter than men, so this difference could simply reflect height differences by sex.

Whereas height has been shown to have a marked association with two hour plasma glucose after the oral glucose tolerance test, fasting plasma glucose and glycated haemoglobin measurements vary very little with height or sex. We should consider whether the oral glucose tolerance test can be replaced with other measures, such as glycated haemoglobin, in everyday clinical practice. This was a topic of debate at this year’s ADA annual conference in New Orleans, and work is already under way to standardise the measurement of glycated haemoglobin. However, as with the oral glucose tolerance test, the validity of glycated haemoglobin needs to be shown across ethnic groups before it is accepted and implemented.

WHO’s warnings in 1965 about the validity of the oral glucose tolerance test across various populations were prescient and deserve continuing attention. The uniform size of the oral glucose load used in this test, even though body size and composition vary, may account for some of the variation in the prevalence of diabetes between men and women and different ethnic groups. Nonetheless, the excess of diabetes in South Asians is marked using other criteria, such as those based on fasting glucose used by the ADA. The complications of diabetes, such as retinopathy and nephropathy, are also greater in South Asians.

Clinicians must be confident that the key tests for diabetes or impaired glucose tolerance are accurate, because the consequences of these diagnoses are considerable and lifelong. Although a false positive result might lead to good advice about diet and exercise, it could also provoke anxiety and adoption of the sick role. A false negative result is potentially dangerous in view of the high levels of cardiovascular diseases and renal dysfunction in South Asians. We must always establish the validity of diagnostic tests across sexes, age groups, and ethnic groups. This still applies to the oral glucose tolerance test and its likely successor, the measurement of glycated haemoglobin.


End of life care in the acute hospital setting
An update of the Liverpool care pathway does much to tackle recent criticisms

Most deaths occur in hospital, yet effective management of dying patients in this environment is challenging. The Liverpool care pathway was developed as a framework to guide practice and extend the excellence of hospice care into hospital, where there was evidence of poor quality care.

An updated version (version 12) of this care pathway was ratified on 2 December 2009. A recent media debate during the consultation period raised criticisms that the pathway is prescriptive and inevitably leads to the patient’s death; it also highlighted concerns about inappropriate sedation and dehydration. The debate
has produced welcome political and professional interest in the care of the dying.

The Liverpool care pathway offers a framework that helps non-specialists manage the dying process, with the aim of ensuring a minimum standard of care for people who are dying. If correctly used it should not hasten a patient’s death. Research from the United Kingdom and international data show that the pathway reduces symptom burden, improves multidisciplinary working, and increases anticipatory prescribing for key symptoms that may develop in the last hours or days of life. It also improves nurses’ confidence in caring for the dying. Two national audits have benchmarked data from acute hospitals. The recent controversy centres on the misdiagnosis of dying; inappropriate withdrawal of nutrition or hydration, or both (potentially leading to poor symptom control and increased distress); and concern about the use of continuous deep sedation to treat agitation (which can be caused by dehydration).

The Liverpool care pathway should be instigated only when death is expected in hours or a few days. However, diagnosing dying is complex—a multidisciplinary team needs to assess the patient and judge how potentially reversible the clinical situation is. Skilled clinical assessment will correctly identify many dying patients, but about 3% of patients will improve on the pathway, and the goals of care will need to be reassessed. The judgment that a patient is dying does not automatically lead to withdrawal or withholding of care, treatment, or interventions, including hydration and nutrition. Good practice involves making decisions on an individual basis.

It is wrong to associate the Liverpool care pathway with euthanasia or physician assisted suicide. Its role is completely distinct—it is a practical tool to help healthcare professionals deliver high quality care when death is inevitable. Unfortunately, the media debate may encourage the public to mistrust the intentions of those wishing to improve care at the end of life and associate the pathway with hastening death. For example, there is no evidence that the pathway leads to inappropriate sedation: the national audit in 2008 specifically looked at prescribing of sedatives at the end of life but found no evidence of excessive prescribing of benzodiazepines or antipsychotics in most hospitals. Even in their last 24 hours, 65% of patients needed no continuous subcutaneous infusion of drugs to control distress from agitation or restlessness; 31% had low doses of drugs to relieve symptoms delivered by subcutaneous infusion and the remaining 4% needed higher doses. (The Liverpool care pathway offers a framework that helps non-specialists manage the dying process, with the aim of ensuring a minimum standard of care for people who are dying. If correctly used it should not hasten a patient’s death. Research from the United Kingdom and international data show that the pathway reduces symptom burden, improves multidisciplinary working, and increases anticipatory prescribing for key symptoms that may develop in the last hours or days of life. It also improves nurses’ confidence in caring for the dying. Two national audits have benchmarked data from acute hospitals. The recent controversy centres on the misdiagnosis of dying; inappropriate withdrawal of nutrition or hydration, or both (potentially leading to poor symptom control and increased distress); and concern about the use of continuous deep sedation to treat agitation (which can be caused by dehydration).

The Liverpool care pathway should be instigated only when death is expected in hours or a few days. However, diagnosing dying is complex—a multidisciplinary team needs to assess the patient and judge how potentially reversible the clinical situation is. Skilled clinical assessment will correctly identify many dying patients, but about 3% of patients will improve on the pathway, and the goals of care will need to be reassessed. The judgment that a patient is dying does not automatically lead to withdrawal or withholding of care, treatment, or interventions, including hydration and nutrition. Good practice involves making decisions on an individual basis.

It is wrong to associate the Liverpool care pathway with euthanasia or physician assisted suicide. Its role is completely distinct—it is a practical tool to help healthcare professionals deliver high quality care when death is inevitable. Unfortunately, the media debate may encourage the public to mistrust the intentions of those wishing to improve care at the end of life and associate the pathway with hastening death. For example, there is no evidence that the pathway leads to inappropriate sedation: the national audit in 2008 specifically looked at prescribing of sedatives at the end of life but found no evidence of excessive prescribing of benzodiazepines or antipsychotics in most hospitals. Even in their last 24 hours, 65% of patients needed no continuous subcutaneous infusion of drugs to control distress from agitation or restlessness; 31% had low doses of drugs to relieve symptoms delivered by subcutaneous infusion and the remaining 4% needed higher doses. The version rightly emphasises that when death is expected, care is considered urgent, as with other acute presentations in hospital.

The supporting documentation that comes with this version is clear and should be a useful aid to clinicians; it emphasises that communication with the dying patient (where possible) and their family is key, and that the views of all concerned should be listened to and documented. This is reiterated in the information provided for relatives and carers. This focus on open communication should help to reduce any suspicions of inappropriate sedation or covert euthanasia. Discussion about the best interests of the patient, including their medical and emotional welfare, will help to ensure that they do not receive more or less treatment than they need to die peacefully and with dignity.

The Liverpool care pathway may lead to poor care because tools are only as effective as the people using them. Professionals instigating and using the pathway need to understand how to diagnose dying, the fundamentals of clinical care, and how to make decisions about end of life care. Implementation of the pathway requires that all workers needed training in end of life care and support from a facilitator or palliative care team. Senior organisational support is also needed so that the Liverpool care pathway is part of a continuous improvement plan for end of life care within any organisation.