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Early adrenaline for cardiac arrest

An old and established treatment still awaiting supporting evidence

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Adrenaline (epinephrine) has been used as a treatment for cardiac arrest since the inception of modern day resuscitation. Despite its widespread use, meta-analysis of existing randomised controlled trials has failed to show any effect or benefit on survival to discharge or neurological outcomes.[1] Some observational studies have even suggested associated harm.[2]

In a linked paper, Donnino and colleagues explored the effect of timing of delivery of adrenaline during in-hospital cardiac arrest.[3] Using data from the American Heart Association Get With The Guidelines registry of in-hospital cardiac arrest, they constructed multivariate logistic regression models to dissect out the effect of early adrenaline on long term outcomes. The analysis focused on a specific cohort of patients—those sustaining a cardiac arrest in hospital with an initial non-shockable rhythm (asystole or pulseless electrical activity (PEA)) on a general hospital ward. It excluded most patients who sustained a cardiac arrest in a specialist clinical area (such as the emergency department or intensive care unit).

Their main finding was a stepwise decrease in hospital survival for every minute that adrenaline delivery was delayed (survival rate of 12% for those receiving the first dose of adrenaline within the first minute, decreasing to 7% after the seventh minute). The finding persisted after adjustment for known confounders and with analysis in three minute intervals with one to three minutes as the reference interval (odds ratio 0.91 (95% confidence interval 0.82 to 1.00; P=0.055) for 4-6 min, 0.74 (0.63 to 0.88; P<0.001) for 7-9 min, and 0.63 (0.52 to 0.76; P<0.001) for >9 min). The findings were robust in a sensitivity analysis that controlled for the time when basic cardiopulmonary resuscitation was started and are consistent with other observational studies.[4 5]

The concept that the time to initial treatment influences outcome was consistent across several clinical emergency settings—for example, thrombolysis for stroke, percutaneous coronary intervention during acute myocardial infarction, and tranexamic acid in major trauma. In cardiac arrest, early cardiopulmonary resuscitation, ambulance response time, and time to defibrillation all influence survival—the longer these treatments are delayed the worse the outcome.

The study has many strengths, including use of data from a large well established in-hospital resuscitation registry. Limitations include the relatively select cohort of patients analysed (20% of the total PEA/asystole cohort) and, despite eloquent statistical adjustments for known confounders, a key limitation of observational studies in general is the potential that unmeasured confounders account for the observed findings.

What unmeasured confounders might explain the findings? Guidelines in place during the conduct of the study recommended that vasopressors (adrenaline or vasopressin) were given immediately after confirmation of asystole or PEA on the monitor,[6 7] yet the median time to administration of adrenaline was three minutes (interquartile range 1-5). The reasons for delayed administration might in themselves account for the findings of this and related studies.

Although the investigators adjusted for the time to starting resuscitation, adrenaline would generally not be given until after arrival of the advanced resuscitation team—thus the delay in administration could simply reflect the late arrival of the advanced resuscitation team.

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Timing has something to do with it

Were there unfavourable patient characteristics that led the resuscitation team to be less aggressive with their resuscitation attempts?[8] Were there difficulties in obtaining vascular access—repeated attempts could lead to harmful interruptions in cardiopulmonary resuscitation. Guidelines at the time of the study recommended that if attempts at intravenous access failed, drugs could be delivered via the intraosseous route or via the tracheal tube. Although the intraosseous route is considered reliable for drug delivery,[9] drugs given via a tracheal tube do not result in consistent blood concentrations. Finally, compliance with guidelines in itself is linked to better outcomes; perhaps delayed adrenaline administration was a surrogate for poorer general cardiac arrest care.[10]

The importance of such confounders was described eloquently by Kudenchuk.[11] In a prospective double blind randomised trial the likelihood of survival to admission to hospital improved dramatically as the interval from ambulance dispatch to administration of the study drug shortened, suggesting a time dependent benefit. In this instance, the study drug was placebo; thus, the effect on survival could not have been a result of the drug but instead the effect of confounders associated with time.

Finally, experimental studies have shown that adrenaline impairs cerebral microvascular blood flow,[12] which could explain why some studies have observed worse long term outcomes in patients treated with adrenaline.[13] It is therefore possible that early administration is simply less harmful than late administration, but no better than no adrenaline at all.

Carry on for now

So what are the implications of this study for clinical practice? We suggest that where healthcare systems include adrenaline as part of their standard resuscitation protocols, it should continue to be given as soon as asystole or PEA is confirmed on the monitor, while high quality cardiopulmonary resuscitation is continued with minimal interruptions in chest compressions. If adrenaline is not part of current treatment protocols, healthcare systems should await the results of ongoing clinical trials. Such studies should endeavour to capture information on the timing of drug delivery to assist in definitively answering the question about how the use of adrenaline and the timing of administration influence long term outcome.

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RESEARCH, p 14

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Use of relative and absolute effect measures in reporting health inequalities: structured review (*BMJ* 2012;345:e5774)

A key area for future research in health policy will be to examine what impact the reduction in the growth of NHS spending has had on health inequalities

Can higher NHS spending in deprived areas reduce health inequalities?

Yes, but housing, education, and employment matter too

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Dealing with the health inequalities associated with socioeconomic status has been a long-standing objective of the National Health Service in England.[1] In a linked article, Barr and colleagues examine the association between NHS resource allocation and changes in "mortality amenable to healthcare" in England.[2]

In 1999, the government introduced a new objective for the allocation of NHS resources in England, which was "to contribute to the reduction in avoidable health inequalities."[3] To help achieve this objective, a health inequalities component was introduced into the NHS resource allocation formula in 2002, which resulted in more rapid growth of NHS spending in deprived areas.

Falling mortality amenable to healthcare

In their paper, Barr and colleagues suggest that the NHS funding formula for primary care trusts (now replaced by clinical commissioning groups) has contributed to a narrowing in the absolute differences in mortality amenable to healthcare between the most affluent and the most deprived local authorities in England. Between 2001 and 2011, NHS spending in the most deprived areas increased by 81% compared with 70% in the most affluent areas (from £1074 (€1319; $1806)/head to £1938/head and from £881/head to £1502/head, respectively). Differences in mortality amenable to healthcare between deprived and affluent areas decreased from 95 deaths in males and 47 deaths in females per 100 000 in 2001 to 54 and 28 per 100 000, respectively, in 2011.

Although it would be encouraging if this reduction in mortality between deprived and affluent areas was a result of targeting NHS resources preferentially at deprived areas, and evidence for continuing with this policy, some caveats in the analysis need to be considered.

Barr and colleagues' study is based on the concept of mortality amenable to healthcare, and there is uncertainty about the extent to which healthcare does reduce such deaths.[4] Although healthcare has been an important contributor

An unsure start

to reductions in mortality,[5] other public policy initiatives may also have contributed to the more rapid decline in mortality in deprived areas that Barr and colleagues identified in their study. For example, the previous Labour government implemented several policies to tackle social exclusion (such as Sure Start and the New Deal for Communities) that may have improved health behaviours (such as smoking and exercise) among poorer people and influenced mortality in the targeted groups. As Barr and colleagues' study is ecological in design, it is not possible to disentangle the effect of higher NHS spending in deprived areas from other government interventions targeting deprived communities. Moreover, death rates from causes of deaths considered amenable to healthcare were decreasing before the introduction of the changes in NHS resource allocation described by Barr and colleagues.[6] These limitations do not, however, detract from the policy implications of the study.

The policy relevance of Barr and colleagues' findings arises from the recent discussion about whether the weighting for age in the NHS resource allocation formula should be increased. The rationale for this is that demand for healthcare increases with age and is highest among people aged 65 and over. Increasing the weighting for age would reflect this higher demand for healthcare by giving greater increases in NHS resources to areas with older populations, which are typically in the south of England and wealthier than areas with younger populations.

However, this proposed change in NHS resource allocation may not reflect the true need for healthcare.[7] For example, the recorded prevalence of chronic diseases is often much lower than the expected prevalence, especially in deprived urban areas.[8] The proposed resource allocation method may also have failed to allow for the under-utilisation of elective and preventive care by people from more deprived areas.[9 10] Hence, using historical utilisation data to determine NHS spending has major limitations. Tackling inequalities is also required in determining the allocation of public resources for healthcare, as well as for other areas of public spending such as education. If deprived areas do not receive more public resources than affluent areas, current health inequalities could be perpetuated or even exacerbated.

The results of Barr and colleagues' study are encouraging and provide evidence for continuing to target NHS resources at deprived areas. However, this may be more difficult in the current political and financial climate as the coalition government has sharply curtailed the growth in NHS spending that England previously experienced: spending on the NHS increased by 8.0% annually between 1997 and 2009, compared with just 1.6% annually between 2010 and 2012.[11] A key area for future research in health policy will be to examine what impact the reduction in the growth of NHS spending has had on health inequalities.[12] This may take some time to do given the delays in data on events such as mortality becoming available and even longer if there are lag effects and thereby a delay between the change in policy and its impact on health status and mortality.

Targeting NHS spending at deprived areas can improve health outcomes and reduce health inequalities. However, although necessary for dealing with health inequalities, NHS spending is only one component of an effective strategy to reduce health inequalities. Other key areas such as housing, education, and employment, and the wider determinants of health inequalities, also need to be dealt with by national and local government and by other public sector organisations.

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- Practice: Identifying and managing deprivation of liberty in adults in England and Wales (*BMJ* 2011;342:c7323)
- Letter: Liberty safeguards in hospital hospital (*BMJ* 2009;338:b2430)

Deprivation of liberty in healthcare

UK Supreme Court judgment has changed the rules

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The right to liberty in UK healthcare has been greatly strengthened this year. In March, the House of Lords Select Committee on the Mental Capacity Act (2005) published a report that severely criticised inconsistent safeguarding provisions for patients without mental capacity who are deprived of their liberty.[1] Later that month, the UK Supreme Court gave judgment in a case "Cheshire West," which involved three adults with severe learning disability and answered the general question "what is a deprivation of liberty?"[2]

The judgment introduces a new disability neutral test—an "acid test"—which aims to ensure that the right to liberty applies equally to people with and without mental incapacity. The test will greatly increase safeguards owed to people without mental capacity in healthcare. Government, and society in general, has an important new challenge.

This decision steers away from the approach to deprivation of liberty taken by the Percy Commission of 1957, which sought legal informality for people without mental capacity who did not object to the offer of healthcare. Cheshire West harks back to the "legalism" of the Lunacy Act of 1845, enacted when society sought to counter the abuses occurring in the private "madhouses" of the day. But this new phase of legalism will have to engage with forms of care that are more familiar and visible than the asylums of old.

How the new acid test will work

The acid test asks two simple questions: firstly, is the person free to leave the place where he or she lives? Secondly, is the person under the complete supervision and control of those who care for him or her? If the first answer is no and the second yes, then safeguards (such as those in the Mental Health Act (1983) or the Mental Capacity Act (2005)) are needed.

If care homes and acute hospitals are looked at through this legal lens, deprivations of liberty are widespread. Yet a healthcare worker's lens is different. The understanding of individual patients' disabilities and their acceptance of offers of care are regarded as important indications of whether a care relationship is working. If it is thought to be working, then identifying a deprivation of liberty is likely to be a foreign instinct.

What, it may be thought, is the ill for which a deprivation of liberty safeguard is the remedy? And what is the effect on a care relationship of framing it in terms of a deprivation of liberty? Two pulls exist and interact in complex ways: the pull to safeguard a human right and the pull to maintain care relationships.

The select committee's criticism of deprivation of liberty safeguards was uncompromising. It identified many concerns, including complexity and uneven implementation; that the safeguards make restrictions "legal" but do not provide real protection; that the nomenclature itself is a deterrent to use; and that there are problems with the supervisory body role, for which the Care Quality Commission has no inspection powers. The House of Lords has indicated that new safeguards should be developed after widespread consultation and adequate parliamentary scrutiny. But following Cheshire West the law has already changed. Clinicians and managing authorities will have to review care arrangements of all potentially incapacitated people in hospitals and care homes with recourse to current law as they await guidance from the state.

PAUL ROGERS/THE TIMES/PA

Two pulls exist and interact in complex ways: the pull to safeguard a human right and the pull to maintain care relationships

Around 200 000 people with dementia live in care homes,[3] and some 40 000 people with learning disabilities live in residential and nursing homes.[4] If the acid test is applied, many will require deprivation of liberty safeguards. On general medical wards, 40% of patients lack capacity to make decisions about care, with higher proportions on elderly care wards and intensive treatment units.[5] Are these patients free to leave? In a large number of cases the answer is no. Are they under the complete supervision and control of those caring for them? The answer, for many inpatients, is probably yes. The acid test does not aim to approve or disapprove of the supervision and control, merely to test its existence. If a deprivation of liberty exists, then—like any other person detained by the state—the patient is owed speedy access to a court to test whether the deprivation is lawful.

In psychiatric hospitals informality will no longer suffice for compliant patients without capacity where the ward environment fails the acid test. Currently, around 40% of patients who lack capacity are not detained under the Mental Health Act (1983).[6 7] Deprivation of liberty will now need to be considered in that group and the interface between the Mental Health Act and the Mental Capacity Act will need renewed attention from government.

The Cheshire West ruling implies that care arrangements for many more people in supported community placements and domestic settings will now amount to deprivation of liberty, with authorisation through the Court of Protection in these circumstances.

Many more mentally incapacitated people now require a legal framework to justify deprivation of liberty under the new acid test. Only 6546 authorisations were granted under the Mental Capacity Act regime in 2012-13.[8] An order of magnitude increase is likely after the Cheshire West ruling.

The challenge now is for the health and justice systems to work together to develop new safeguarding provisions that make clinical sense and provide genuine safeguards for the most vulnerable. The focus can now shift from the acid test to the subsequent action of considering whether a patient's circumstances are necessary, proportionate, and in his or her best interests. To miss this opportunity and to end up with a costly but largely administrative safeguarding regime would be unacceptable. The purpose of the safeguards must not be lost in translation between our justice and health systems.

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The "Saatchi bill" will allow responsible innovation in treatment (*BMJ* 2014;348:g2771)
Views and reviews: Withdraw Saatchi's quackery bill (*BMJ* 2014;348:g2974)

Why there is no legal or medical justification for the Saatchi bill

More a memorial to deeply missed partner than a contribution to improving cancer care

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Consultation on the Medical Innovation (Saatchi) Bill attracted 18 000 responses, which are being analysed by the Department of Health.[1 2] The health secretary, Jeremy Hunt, the prime minister, and several cabinet colleagues support the bill,[3] which may become part of next year's proposed legislation. Much medical opinion has been against the bill, but several eminent doctors and judges favour it.

The original bill was proposed by Maurice Saatchi, whose wife died from a rare form of ovarian cancer in 2011, aged 67. He believes her death was wasted because it did not help advance scientific understanding.


GERAINT LEWIS/ALAMY
Wonderful life; unnecessary bill

She does not seem to have been denied any specific treatment. Her cancer was "advanced, malignant and inoperable." Saatchi described her radiotherapy and chemotherapy as "degrading and ineffective."[4 5] He believes that she received "standard treatment." This is the target of the bill, which sees current law favouring it over innovative treatment. Commentary supporting the bill states: "Under present law, any deviation by a doctor from standard procedure is likely to result in a verdict of guilt for medical negligence." It continues, this is why "there is no cure for cancer."[1]

These are major overstatements. Common law rests on the Bolam principle, which states that a doctor is not negligent in prescribing an unproven experimental treatment if it is supported by a responsible body of medical opinion.

This "professional consensus" defence already accommodates innovation by minority opinions. For example, professional consensus approved a 1% minority opinion in favour of spinal surgery (by spinal surgeons) despite a large majority of neurosurgeons disapproving of the surgery (De Freitas *v* O'Brien [1995] Med LR 108).[6] Doctors can prescribe unlicensed drugs and, in extreme cases, untested drugs awaiting approval, as they did for patients with variant Creutzfeldt-Jakob disease (Simms *v* Simms [2002] Fam 83).[6] The Department of Health has not suggested that law is an obstacle to medical innovation.

Nevertheless, the bill seeks to clarify the legal freedom of doctors by encouraging "responsible innovation," based on specific criteria. The second draft of the bill included notable changes—expanding its scope to cover all diseases and requiring agreement from the "doctor's responsible officer," rather than relying on the opinion of a multidisciplinary team. Michael Rawlins has supported the bill owing to these changes but has proposed that any such treatments be registered so that others may learn.[7]

Much of the opposition to the bill has been based on it being unnecessary, given the freedoms in existing law. Central to arguments in favour have been the views of Harry Woolf and Elizabeth Butler-Sloss,[2] who, on the basis of their judicial experience, support a change in the law.

The most thorough discussion of the legal aspects of the bill is by the Saatchi campaign's barrister.[2] Notably, he found "little to demonstrate that innovation is stifled by the risk of being sued." He concludes that the bill did not "effect a substantive change in the law" but it may influence how doctors perceive the law. This is a major concession to those who dispute the need to change the law. If doctors' perceptions are the problem, besides changing the law, softer solutions are available, including clarification and codification by professional bodies.

The other argument put forward by the bill's supporters involves the increased number of medical negligence cases in recent years.[2] This it is claimed is part of a "growing bias against medical innovation." This assertion is contestable, but even if true, this rise started in the mid-1990s,[8] encouraged first by Legal Aid and then by contingency fee arrangements. Recent limits on funding (including referral fees) mean that the number of cases is likely to fall sharply.

The Saatchi campaign's barrister found "little to demonstrate that innovation is stifled by the risk of being sued." He concludes that the bill did not "effect a substantive change in the law"

The health secretary has committed "that the government will seek to legislate at the earliest opportunity, subject to the results of the consultation."[3] In this he should be guided by the analysis of cases identified in the consultation. The consultation responses of 22 organisations did not identify a single instance of existing law deterring a doctor from innovation.[9] These responses also identify the risk of making the doctor's decision more subjective, the weakness of reliance on the "responsible officer," the shift of risk to patients from any sponsoring organisation and diversion of attention from relevant clinical trials.

Few case studies are well documented, but one—the Child B case in 1995—shows the complexities.[10] The proposed experimental chemotherapy may have extended the patient's life for some months, but the treatment changed several times, was expensive, caused side effects, and ultimately, the patient died. The law was no barrier; the episode did not advance science.

Collating data on cases treated by innovative treatments is key to learning from them. How this would happen remains unclear, and the detail needed is likely to be onerous. If the bill proceeds, the Department of Health might clarify how best to collect relevant data.

That this bill has got so far is testament to Saatchi's campaigning skills and, perhaps, the extent of his grief. But the lack of support for his two key arguments for change is striking. Even his own legal advice states that the bill leaves existing law unchanged. Numbers of medical negligence cases are likely to fall. The legal case for reform is weak. If the bill becomes law, it may be more as a memorial to a deeply missed partner than as a contribution to improving cancer care.

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