comment

"We must recognise conflicts of interest's pervasive harm" **CHRIS VAN TULLEKEN ET AL**
"Not formally in the NHS? Schrödinger's GPs are really angry **HELEN SALISBURY**
PLUS David Oliver on the PA impasse

THE BOTTOM LINE Partha Kar

Leng's review of physician associates is welcome

Finally, we're here. After months of heated debates, social media uproar, royal colleges in turmoil, and the reputation of many national organisations being questioned, the worm has turned. The health and social care secretary, Wes Streeting, has called for a review of how physician and anaesthesia associates are deployed in the NHS.

The review's chair, Gillian Leng, has a strong reputation and is well placed to conduct it. Since the brief is to look at data neutrally and to reach a decision about whether these roles are a cost effective use of taxpayers' money, the former chief of NICE is as good as it gets.

So, what next? One thing is to allow open communication and to ensure there is a genuine desire to investigate this thoroughly. This issue won't just go away. Doctors have spoken out against a succession of leaders who have failed to hear them. This has resulted in a lack of trust, and the attempts to silence them haven't worked.

I'd ask the review to consider a few things around safety and cost. A clear steer on national scope is needed: it's untenable for a dependent health profession not to have one. Locally defined scope causes inconsistency and must end. Supervisory lines need to be clear, and this shouldn't involve leaning on resident doctors.

We also need a GMC register for PAs that clearly states who their supervisors are. And we must consider the cost effectiveness of their roles. In a system where treatment is rationed, to have a role where the scope of work is below the banding scale for other NHS staff is unfair and a waste of taxpayers' money.

Do associates have a role? Possibly so, if they keep to the narrative of professionals there to help doctors by decreasing the administrative burden, so doctors can deliver care based on their unique clinical training.

A role built to compete with doctors, but with less training and more risk to patient safety, is not what the system needs. A two year condensed training course in any form cannot provide more expertise than five years in medical school: if it did, we'd need to scrap medical schools and refund many doctors' student loans. The rhetoric of "we don't have enough doctors, so we need other professionals" is false. We do have enough doctors; what we don't have is enough training posts.

I raised these queries in a column about a year ago, time that has been wasted in further acrimony, with evidence of harm documented by high profile cases.

There's also a wider question about those who welcomed the NHS workforce plan and its expansion of associates without relevant scrutiny or due diligence. The government has called for this review on a part of the workforce that's been championed by NHS England's Workforce, Training and Education Directorate (formerly Health Education England), which has spent a year ignoring calls for a pause in expanding these roles. This raises questions about leadership accountability—or lack of it.

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A role built to compete with doctors, but with less training and more risk to patient safety, is not what the system needs

OPINION Chris van Tulleken, Nigel Rollins, and Rebecca Coombes

Conflicts of interest: moving towards zero tolerance

Harmful industries still exert influence; robust change is required

In the 1950s, smoking was proved beyond doubt to cause cancer and yet efforts to curb this pandemic were stalled over the next half century by a network of individuals and institutions with competing interests. The industry paid doctors, academics, charities, and policy makers to dilute and distort the science and public health messaging.

By the 1980s, the largest tobacco companies bought the largest food companies and used the same methods to create a food environment where poor diet has overtaken tobacco as the leading cause of early death globally.

Food and tobacco are just two of the industries that use their economic power to evade effective regulation; pharmaceuticals, alcohol, gambling, and fossil fuels, among others, have the same commercial incentives and obligations and directly impact human and planetary health. The World Health Organization has defined these commercial determinants of health as "…private sector activities that affect people's health, directly or indirectly, positively or negatively."

To varying degrees, all these industries fund and partner with those that would regulate them—from de facto regulators, including charities, press offices, health professional associations, academic departments, doctors, and influencers, to formal regulators such as the government and guideline committees.

This funding creates competing interests because the interests of these industries conflict with the interests of public health. Many of the corporations in these sectors are "financialised" and have obligations to prioritise profit and growth, and thus they are not suitable partners for change.

Harms to health versus taxation

In the case of food, alcohol, and tobacco, the economic costs associated with the harms to health substantially exceed the revenue generated from taxation. Despite these issues, influential national and local health advisory committees on food, alcohol, and pharmaceuticals commonly include experts with financial conflicts of interest.

Meanwhile, companies in these sectors invite senior clinicians and academics to be on advisory boards to portray impartiality and build credibility. These actions reflect the important and trusted role of health professionals in society and why they are high value targets of industry marketing strategies.

Each sector presents unique challenges and requires specific approaches. The pharmaceutical industry is more regulated than food or alcohol, but it has promoted competing interests with guidelines committees, advocacy groups, clinicians, and academia that work against patients' interests.

Moves towards more transparency in medicine have failed. The pharma industry's disclosure scheme, Disclosure UK, allows doctors to remove their name from annual declarations of payments and gifts. Unsurprisingly, many of these doctors opt to continue to accept actual or in-kind remunerations (including trips to conferences and meetings, speaker fees, hospitality, meals, and gifts) away from the public gaze.

Mandatory disclosure does not reduce or mitigate against competing interests. Last year in the US, where any payments must be declared, $2.29 bn (£1.83 bn) in non-research payments was made to physicians from pharmaceutical companies.

In the UK, a requirement for comprehensive registers of interest at NHS trusts failed and a high profile call for all UK doctors to submit their declarations of interest to a public register

ACUTE PERSPECTIVE David Oliver

The current stand-off may leave physician associates stranded

There has been much controversy around plans to expand the numbers of medical associate professionals (MAPs) in the NHS—mainly physician associates (PAs) but also surgical care practitioners and anaesthesia associates.

On 20 November the government commissioned a review into the associate professions, focusing on safety and their appropriate roles within health teams. The health secretary, Wes Streeting, said that he aimed to end "toxic debate" over the issue.

The impasse could leave MAPs, especially PAs not already in post, stuck with limited prospects, while those in post face greater scrutiny over their scope of practice.

The NHS workforce plan, published in June 2023, was explicitly structured around training and retaining more staff and "reforming" how staff work, the mix of skills in teams, and a proposed shift towards more community models and digitally enabled care. Delegation or expansion of clinical professional roles, role substitution, and the creation and expansion of newer roles were all part of the thinking. Meanwhile, the long expected GMC plan to regulate PAs will come into force in December.

I can't see trusts or GP partnerships wanting to offer many jobs to new PAs

The NHS workforce plan sets out current training numbers and future expansion across all clinical professions. For MAPs, total training posts in universities were 1417 in 2022, with a planned increase to 1687 by 2028 and to 1802 by 2031. When compared with plans for expanded numbers in medical, nursing, allied health professional, and advanced care practitioner training, even if all those MAPs find employment they'll be a very small percentage of the clinical workforce.

Yet their presence has become a lightning rod for a range of other issues—not least the qualified GPs unable to find employment in practices that use ringfenced money to employ PAs, as well as the bottlenecks in postgraduate medical training, resident doctors' dissatisfaction with their access to training, and the presence of unregistered, dependent practitioner PAs on medical on-call rotas or other roles that would usually require registered professionals, including review of undifferentiated patients in primary care.

I'm not sure NHS England's Workforce, Training and Education team anticipated this backlash. When I sent them a freedom of information (FOI) request earlier this year to obtain their risk register for the workforce plan, the document was short and scant. I also asked whether they had a specific risk assessment around the MAP expansion, and they said there was none, as MAPs were already an established part of the workforce.

I sent the same team FOIs about the consultation launched in January 2024 on proposals for four career grades of PAs that

Conflicts of interests create bias, which we might call co-option or corruption

held by the GMC has been ignored.

Journal declarations can detail some competing interests but standards vary, leading to misleading or partial statements, often hidden in footnotes. Similarly, medical royal colleges do not always disclose publicly the millions of pounds they receive from drug and medical device companies. No accurate collection or reporting of pharma payments to NHS trusts is published. We need a reset.

Conflicts of interests create bias, which we might also call co-option or even corruption. They act in several ways to impact public health, health policies, and patient care. They affect the behaviour and beliefs of individuals and institutions. These conflicts shape research agendas and determine which questions are asked and which ones are not. They then affect the outcomes of that research. Conflicts affect what we and our children eat and drink, which drugs and devices are prescribed, and the research that is undertaken, published, and reported.

Even when an institution or individual can remain independent of the interests of their funders, these competing interests silence critique and protect the reputations of corporations that market products known to cause harm. Additionally, these biases erode trust in science, medicine, and public health.

What needs to happen

Change has to be intentional, systematic, evidence based, and robust. The onus for action is not with industry which, because of its responsibilities to shareholders, is unable to prioritise public health.

All institutions and individuals who have the stated aim of improving human health—health authorities, research funders, medical schools, health professional associations, charities, and individual practitioners, to name just some—must first recognise the pervasive harm that conflicts of interest cause.

Governments must set the standard and lead by example. Terms of engagement that end actual and perceived competing interests should be established while not precluding the possibility of discussion with these industries. Advisory committees, regulatory bodies, and harm reduction strategies must be conflict free.

A change in culture among health professionals and in those making decisions about policy and investments is needed. It is accepted today that doctors, universities, and institutions should not receive funding from the tobacco industry. This principle needs to be widened to other industries whose products or marketing also harm or undermine health. Medical, nursing, and pharmacy schools must prepare trainees to recognise competing interests and respond ethically and effectively.

Medical and science journals can implement stricter competing interest policies and make competing interest statements more visible but also consider introducing stricter, zero tolerance policies on clinical education articles that are designed to protect patient care.

The financial incentives that drove the tobacco industry to create a pandemic of smoking related disease are common to many other industries. The first step in limiting the harms caused by commercial determinants is to end their competing interests with those who would regulate them.

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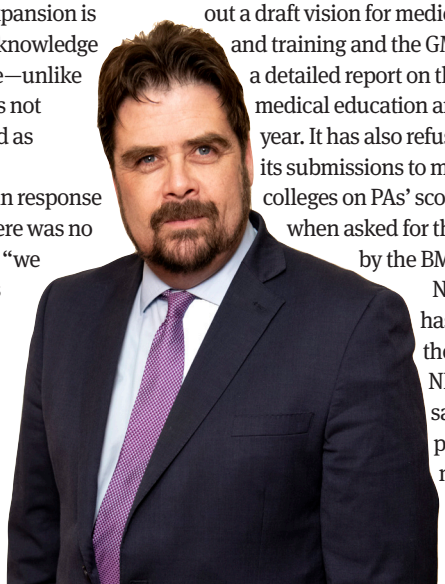
look suspiciously like grades for medical doctors. They refused it on the grounds of public interest and the preparation of an ongoing report.

The workforce plan includes considerable detail on the modelling and rationale for the expansion of medical, nursing, and allied health professional training numbers and posts. But the rationale for PA expansion is absent. Nor do PAs have a set of knowledge and skills distinct from medicine—unlike the other clinical professions. It's not clear what unique value they add as dependent practitioners.

Meanwhile, the GMC told me in response to a separate FOI request that there was no risk assessment for this work, as "we do not produce risk assessments but instead continually evaluate risk"—a bizarre admission for a national statutory professional regulator. It also refused to release details of the public consultation responses on the rules, standards, and guidance for regulation of PAs and AAs, not only in response to my own FOI but to those from other doctors.

The GMC's argument is that those responses form part of the research for a report that will soon be published. It advised me it wasn't responsible for workforce issues, even though its medical director, Colin Melville, has set out a draft vision for medical education and training and the GMC publishes a detailed report on the state of medical education and practice each year. It has also refused to release its submissions to medical royal colleges on PAs' scope of practice when asked for the information by the BMA.



NHS Employers has followed the GMC and NHS England in saying scope of practice is a local matter, not for determination by central agencies: they don't accept the BMA's guidance as valid or binding.

We await the impact of the new independent review. PAs themselves have become scapegoats for a whole range of other concerns doctors have about their own careers, and I feel as though they've been misled into imagining a secure future career. There will now be so much concern about safety, risk, and reputation that I can't see NHS trusts or GP partnerships wanting to offer many jobs to new PAs.

NHS England and the GMC clearly regard all the criticism and campaigning as inconvenient, unwelcome, and vexatious. But this has happened on their watch, as has the failure to plan postgraduate medical training or to fund the GP contract properly. They now have a responsibility to fix it—not wash their hands of a problem they created, enabled, and worsened.

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PRIMARY COLOUR Helen Salisbury

If GPs aren't in the NHS, what are we?

One of the huge attractions of practising medicine in the UK is that we can make our treatment decisions according to our patient's clinical need, not their ability to pay.

Most of the time, I don't need to tailor my clinical advice to what my patient can afford or whether they're insured—although I do have to think about money, about the capacity of the NHS as a whole and its finances. This is one of the many reasons I'm proud and happy to be a GP in the NHS.

I was therefore shocked to hear the health secretary, Wes Streeting, tell ITV's *Good Morning Britain* on 13 November that GPs are not formally part of the NHS. What have I been doing for the past two and a half decades? The status of GP partnerships as private businesses with a single contract to the NHS was brought to the fore by the budget on 30 October. Not only are GPs ineligible for any reimbursement of the increased cost of employers' national insurance contributions, on the grounds that they're private businesses, but they're also not entitled to the help small businesses can get from the Treasury for extra employment costs, on the grounds that they provide public services. We are Schrödinger's GPs.

But although we're not "formally" part of the NHS, apparently we're "a valued member of the NHS family," said Streeting in a letter to Katie Bramall-Stainer, chair of the BMA's General Practitioners Committee for England. It all seems a bit confused, and, despite the letter's warm words, it gave no concrete reassurance that money would be found specifically to cover this new cost in the £22.6bn awarded to the NHS.

This ongoing uncertainty has many unfortunate consequences. Some practices will be planning reductions in staffing and patient services, while others are considering handing back their contracts altogether as this latest cost pressure tips them over the edge into unviability. Some GPs are suggesting that, if we're not part of the NHS, we shouldn't be subject to restrictions that prevent us from selling our services. And although some doctors would undoubtedly relish the freedom to offer private services, most of us recognise that this would increase inequalities and widen the health divide between rich and poor.

Probably the biggest impact locally is that GPs are really angry. Many who were only half heartedly taking part in the collective action designed to put pressure on the government to resource general practice appropriately have discovered a new appetite for industrial action. Streeting had an opportunity to cool tempers and build bridges ahead of last week's conference of local medical committees. It's a great shame for our patients, and for our profession, that he squandered that chance.

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GPs who were only half heartedly taking part in collective action have discovered a new appetite for industrial action

LATEST PODCAST

Neutrality in conflict and antimicrobial resistance

This podcast comes from the World Innovation Summit for Health, where *The BMJ* was a media partner. The meeting focused on conflict, equity, and resilience. Christos Christou, international president of Médecins Sans Frontières (MSF), talked about the difficulty and importance of maintaining neutrality in conflict zones, and what that means to them:

"When you are independent, you can impartially assess the needs of people and say, 'I'm here for everyone. I don't take sides. My hospitals are neutral. The patients are patients.' Even if we are taking care of your enemies, we are not your enemy—that's how we interpret neutrality. But at the same time, our two main pillars are medical action and bearing witness—telling the stories of people and carrying their testimonies. So neutrality in MSF and in all of these contexts means a lot of things, but neutrality does not mean silence."

Ara Darzi, surgeon and executive chair of the conference, also joins to talk about antimicrobial resistance, and how diagnostics and a small funding commitment could head off the problem:

"Science alone is not going to fix this problem, but science is critical in helping us get over some of the big challenges facing us. One of these areas is the opportunities we have when it comes to artificial intelligence. We hope it will enable quicker diagnostics, new drug discovery, and more precise prediction in tailoring the right antibiotic at the right dose and the right time. The second one is diagnostics. We need point-of-care diagnostics. These technologies are available. They could be in clinics. We need to disseminate those innovations. We spend 90% of our purchasing budget on medicinal products and 10% goes on diagnostics. That ratio has to change."

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Kelly Brendel, deputy digital content editor, *The BMJ*

ANALYSIS

Fragile promise of psychedelics in psychiatry

Cédric Lemarchand and colleagues highlight weaknesses in the evidence on efficacy and safety of hallucinogens and question the use of expedited regulatory pathways

KEY MESSAGES

- There has been renewed interest in the use of psychedelics for treating mental health problems
- Regulatory agencies have approved several psychedelics using accelerated procedures that require lower levels of evidence
- Published studies often have problems such as overstated benefits, small sample sizes, and short follow-ups
- Additional problems include conflicts of interest, lack of standardisation on safety outcomes, and functional unblinding
- More rigorous research and higher ethical standards are needed to protect patients

The US clinical market for ketamine, estimated at $3.1bn in 2022 and expected to expand at 10.6% a year until 2030,[1] is just one of many signs of renewed interest in the use of psychedelics to treat psychiatric conditions.[2] Various mind altering drugs have already entered the market, including esketamine nasal spray, which the US Food and Drug Administration (FDA) approved in 2019. And in 2022 the Australian Therapeutic Goods Administration (TGA) allowed psilocybin and 3,4-methylenedioxymethamphetamine (MDMA) to be prescribed by authorised physicians for psychiatric conditions such as depression and post-traumatic stress disorder (PTSD). The decision was taken despite an independent scientific report commissioned by the TGA advising against authorisation because the certainty of evidence for benefits was low or very low.[3]

Psychedelics, the lay term for substances classified as hallucinogens, have various targets and distinct purported mechanisms of action. For instance, psilocybin is a serotoninergic agonist, whereas esketamine is a N-methyl-D-aspartate (NMDA) glutamate receptor antagonist, although its effect is also attributed to synaptic plasticity. Mystical experiences have also been reported as a mechanism of action.

Nevertheless, hallucinogens as a group are often understood as "a new paradigm of care for mental health."[4] While many countries, including the UK, Japan, Indonesia, Saudi Arabia, Singapore, Russia, and China, have maintained relatively strict regulatory standards for hallucinogens, more relaxed approaches in the US, Australia, and Europe are hindering repeated calls for a critical evaluation of the evidence.[2 4]

Regulatory challenges

The clinical use of hallucinogens began after Alfred Hofmann accidentally discovered the psychotropic effects of LSD while working at Sandoz in 1943.[5] The drug was initially hailed as a cure for mental health problems, but enthusiasm waned because of negative clinical outcomes, controversial experiments by Timothy Leary, and failed military research.[6] Sandoz stopped producing LSD and psilocybin in 1965.[7] Furthermore, the tightened standards for drug evaluation following the thalidomide scandal, the Kefauver-Harris Drug Amendments Act in 1962[8] and the Comprehensive Drug Abuse Prevention and Control Act of 1970, effectively ended research on hallucinogens in the US.

Fifty years later, the renewed interest in hallucinogens comes at a time when the big drug companies have reduced research into psychopharmacology, leaving patients and clinicians with psychotropic drugs of limited efficacy[9] and unmet medical needs that they hope hallucinogens will fulfil. Simultaneously, regulatory agencies are deploying expedited pathways more frequently,[10] resulting in a lowering of approval standards worldwide. However, the evaluation of hallucinogens comes with unique methodological and regulatory challenges. In the US, the FDA must assess efficacy through "adequate and well controlled trials." This is challenging for hallucinogens because of functional unblinding, when participants often know their group. Although blinding isn't always essential, it is a crucial safeguard, especially for subjective outcomes[11] and when there are strong participant expectations or investigator conflicts of interest. The FDA and European Medicines Agency (EMA) are therefore developing guidelines to deal with pitfalls such as unblinding, suitability of control groups, and safety concerns (box 1).[12 13] Furthermore, because hallucinogens are often combined with a psychotherapy component, it is difficult to separate the effects of the drug from the therapeutic context, complicating comprehensive evaluations and product labelling (box 2).

Hallucinogens as a group are often understood as "a new paradigm of care for mental health"

Changing authorisation standards

To address the unmet need for severe and treatment resistant mental illness, the FDA has encouraged research on hallucinogens by designating some as breakthrough therapies. The designation was introduced to allow an expedited review process for drugs "intended to treat a serious condition [where] preliminary clinical

Box 1 | FDA and EMA recommendations for trials of hallucingens[12 13]

Characterisation of clinical pharmacology

- Assess potential drug-drug and drug-disease interactions
- Evaluate inter-individual variability in drug metabolism caused by age, sex, diet, etc
- Define dose-response relations
- Explore connections between acute experience and long term effects for both efficacy and safety

Study design

- Address functional unblinding by using independent and blinded raters and questionnaires to minimise bias from perceptual disturbances
- Include psychedelic-naive patients to reduce expectancy bias and regularly assess patient expectations
- Use active placebos—that is, placebos that produce effects that may convince the person being treated that they are receiving the drug under study
- Triangulate evidence using dose-response data and evidence from studies with inactive control treatments that can help to contextualise safety findings
- Evaluate effects over at least 12 weeks and monitor long term symptom recurrence over a year

Safety

- Identify and manage adverse events (eg, anxiety, headaches, tachycardia)
- Set monitoring requirements before, during, and after the studies
- Exclude patients with pre-existing conditions (valvopathy or pulmonary hypertension) and explore risks of 5-HT2B (serotonin) receptor agonists (assess valve structure and function and pulmonary artery pressure). Evaluate the potential for misuse
- Ensure the healthcare system can prevent overdose for both patients and non-patients

evidence indicates that the drug could demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)."[14] This means that even a low level of evidence suggestive of efficacy is deemed sufficient to consider the treatment as promising for an unmet medical need. Companies often use expedited development and regulatory review pathways to accelerate regulatory approval of expensive cancer drugs despite a lack of robust evidence of their efficacy and safety. However, in a 2016 survey of around 700 physicians, a quarter wrongly believed that drugs receiving breakthrough designation were safer than previously approved treatments.[15]

The FDA granted esketamine breakthrough designation for "treatment resistant depression," even though there was no consensual definition of the condition. In addition, the FDA lowered the regulatory threshold by not enforcing its decades old requirement for at least two positive initiation trials.[16] Of the three short term (four week) initiation trials, only one showed a significant benefit over placebo. For the first time, a maintenance trial was accepted in place of a second positive initiation trial, despite the risk that such trials overestimate treatment effects.[9]

Esketamine is not an isolated example. The FDA used the breakthrough therapy pathway to approve bupropion plus dextromethorphan for major depressive disorder and also for assessment of MDMA for post-traumatic stress disorder, LSD for anxiety, and psilocybin for depression. In Europe, although the EMA followed the FDA's decision on esketamine, several European health technology assessment bodies, including the French National Authority for Health and UK National Institute for Health and Care Excellence (NICE), refused authorisation because of important gaps in the evidence (such as questionable clinical added value or insufficient data on long term efficacy and safety). Of note, NICE's decision not to recommend esketamine nasal spray for treatment resistant depression was based on both clinical efficacy and cost effectiveness,[17] highlighting that agencies include other considerations beyond clinical evidence.

Box 2 | Steps to establish trial effects are not due to psychotherapeutic components[12 13]

- Avoid using in-session therapists or monitors in post-session psychotherapy to prevent them deducing treatment assignments and inducing performance bias
- Manage high expectancy by limiting the potential for psychotherapeutic interventions to increase expectations and performance biases
- Compare psychedelic drugs with psychotherapy or psychological support alone, possibly using factorial designs
- Explore the maintenance of effects and the need for repeated sessions and follow-up psychotherapy, with or without adjunctive pharmacological treatment

Inconsistencies in reporting

Given the hopes it has raised, research into hallucinogens has been a hot topic, with many new players. Alongside prominent drug companies such as Janssen (esketamine), many smaller companies are sponsoring studies, including Compass Pathways (psilocybin), Axsome Therapeutics (dextromethorphan), and Lykos Therapeutics, which was established by the non-profit advocacy organisation Multidisciplinary Association for Psychedelic Studies. The research agenda is rapidly growing. A search of interventional studies registered on ClinicalTrials.gov shows trends typical of products in the early phases of development with registered study information often poorly described and inconsistent, small sample sizes, and short follow-ups.[18]

Inconsistencies are also evident in published articles on hallucinogens. For instance, *JAMA Psychiatry* published an open label psilocybin study without a control group as a "non-randomized controlled trial"[19]; a study published in *eClinical Medicine* used "double blind" in the title, while the text reported clear and strong evidence of unblinding[20]; and a meta-analysis on psilocybin published in *The BMJ* received an expression of concern just three days after publication because of likely inconsistencies and errors.[21]

Adequacy of blinding is often not properly assessed in pivotal studies. For esketamine, functional unblinding was not specifically assessed, even though esketamine has been shown to increase the risk of dissociation sevenfold.[22] Functional unblinding was also not formally assessed in the first pivotal study of MDMA assisted psychotherapy used for a new drug application to the FDA.[23] However,

the presented data suggest that 81/90 (90%) participants may have correctly guessed which treatment they received at the end of the intervention.[24] In the second pivotal study used for FDA approval, the article misleadingly stated that the trial was "double blind" and that "not all participants correctly identified the treatment that they received." However, the supplementary data show that 94% of the patients assigned to MDMA correctly guessed their treatment assignment, versus 20% who thought they received MDMA in the placebo group.[25] In addition to the problem of functional unblinding, a report from the Institute for Clinical and Economic Review, which conducts independent assessments of health interventions in the US, concluded that it was "not able to assess the frequency of misreporting of benefits and/or harm and thus the overall net benefit balance with MDMA." It also noted that "concerns have been raised by some that therapists encourage favourable reports by patients and discourage negative reports including reports of substantial harm, potentially biasing the recording of benefits and harm."[26]

There is also evidence that the media have overstated the benefits of hallucinogens. An example is an article in the *Guardian* suggesting that psilocybin was "a more successful treatment for depression than a typical antidepressant,"[27] although the study it was reporting on found no significant difference on its primary outcome.[28] In Maryland there were misleading, possibly false, claims in online direct-to-consumer advertising for the off-label use of ketamine.[29] Industry influence is a risk even in the scientific literature. For example, a *Nature* Outlook on psychedelic medicine published in 2022 was sponsored by the biotechnology company Atai Life Sciences, which conducts research into several hallucinogens and novel 5-HT2A receptor agonists; it comprised 12 news features, one editorial, and a "sponsor feature."[30]

Safety concerns

In contrast to well established drug classes, hallucinogens have various proposed mechanisms of action, and their long term effects are not fully understood. The potential for harm and serious adverse events from long term use of hallucinogens would not be evident in short term trials. Pharmacovigilance suggests that esketamine could be linked to suicidal behaviours.[31] A similar signal is observed for psilocybin, suggesting that it could increase serious adverse events, especially suicidal ideation and behaviours.[32] Cardiovascular problems are to be expected, especially in vulnerable populations, as esketamine increases the risk of hypertension. While some of these events were observed during drug development, suboptimal reporting of safety issues in journal publications may have led to underestimation.[33] Furthermore, 5-HT2B agonists such as psilocybin increase the risk of valvular disease.[12] Ketamine and its derivatives are known to increase the risk of urinary disorders, and severe ulcerative cystitis has been documented.[34] The potential for abuse or misuse must also be considered. For example, recreational use of ketamine is increasing in the US, alongside poisoning[35] and legal seizures.[36]

Companies often use expedited development and regulatory review pathways to accelerate regulatory approval

Beyond the drug related adverse events, the psychotherapeutic component of "psychedelic assisted psychotherapy" introduces additional safety concerns. Mind altering drugs place patients in a state of heightened vulnerability and potentially increased risk of harm. For example, legal proceedings are under way involving therapists accused of sexual assault in a clinical trial of MDMA.[37] That such events occurred in closely monitored clinical trials, where best practices are theoretically ensured, is particularly concerning and raises serious concerns about the potential risks of use in everyday clinical practice. Despite these risks, insufficient safeguards have been put in place since Australia legalised psilocybin and MDMA to treat depression and PTSD.[3 38]

Moving forward

Growing numbers of hallucinogenic drugs are being marketed for treatment resistant disorders. According to a 2023 narrative review in *World Psychiatry*,[39] treatment resistance could now affect up to 55% of people receiving antidepressants. In the context of a global shortage of clinicians, ensuring widespread availability of treatment facilities with appropriately trained and licensed professionals to guarantee medical oversight and safety precautions is a challenge. In addition, these new treatments will probably require multiple therapy sessions at considerable cost—estimates in Australia are around $25 000 (£13 000; €15 000; $17 000) per treatment[40]—which is likely to limit accessibility and exacerbate (mental) health inequalities.

Because the stakes are so high, it is imperative that the benefits of hallucinogens outweigh the risks associated with relying on low quality evidence. To guarantee that hallucinogens are rigorously vetted before endorsing them as safe and effective treatments, medical journals must appraise the evidence more critically, fully account for limitations, avoid spin and unsubstantiated claims, and correct the record when needed. For example, *Psychopharmacology* retracted three studies on MDMA because of data integrity concerns and lack of transparency about some of the authors' conflicts of interest.[41] Health authorities must require standard regulatory pathways over accelerated ones. Otherwise, they set a concerning precedent and encourage research of degraded quality, whose numerous inconsistencies are not up to standards. Regarding MDMA assisted therapy, the FDA turned down the application.[41] It remains to be seen whether this decision will prompt the generation of higher quality evidence in hallucinogen research.

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LETTERS Selected from rapid responses on bmj.com

LETTER OF THE WEEK

Deadly nitazenes: a 2024 update

In England and Wales, drug related deaths increased in 2023 to the highest level since 1993 (Seven Days in Medicine, 2-9 November). In England, we have seen a sharp rise in deaths involving nitazenes, a group of potent synthetic opioids. These compounds are being found in street heroin and cocaine, seized powders, counterfeit tablets purchased online, and in vaping liquids.

We conduct toxicology analysis on behalf of coroners. From 1 January to mid-October 2024 our unit detected nitazenes in just under 100 postmortem cases. The Office for Health Improvement and Disparities reported 179 deaths associated with nitazenes across England between 1 June 2023 and 31 May 2024. Our unit's data are in addition to these deaths. This indicates that deaths involving nitazenes are being underestimated in government reports and that nitazenes are a major public health concern.

We recently encountered two deaths involving a new nitazene: N-pyrrolidino isotonitazene. Both cases were known to purchase drugs online and were in possession of unlabelled green tablets, one of which tested positive for N-pyrrolidino isotonitazene. When nitazenes first started being detected in deaths, there was always evidence of heroin or cocaine use too. But the recent cases were negative for heroin and cocaine use, indicating that the user group is broadening. To our knowledge, there have been no cases in the published literature of N-pyrrolidino isotonitazene being identified in a death.

Deaths related to nitazenes are increasing, and with the rapid emergence of new nitazenes, identification of these compounds is becoming increasingly challenging. As the user group for nitazenes is broadening, public awareness strategies need to be updated. The wider population now needs to be warned of the risks associated with purchasing drugs online. Education could be delivered through media outlets, schools, and colleges, as well as medical professionals.

Limon K Nahar, senior toxicologist; Rebecca Andrews, deputy head; Sue Paterson, head, Toxicology Unit, Imperial College London

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HOW TO GET STARTED IN MEDICAL LEADERSHIP

Skills, failures, and shortlisting

Eddy and colleague's article is an excellent resource for resident doctors to encourage leadership experience (Practice Pointer, 19 October). Leadership is a key skill for all doctors. The GMC states that, whatever their role, doctors must "demonstrate effective team working and leadership."

Although leadership skills are needed at all grades of medical training, they become more important with increasing seniority. Leadership is a skill that can be practised and improved; doctors in senior leadership positions are associated with better organisational performance.

Leadership failures have been implicated in high profile safety cases. The importance of trainees was emphasised in the Mid Staffordshire inquiry, stating: "Trainees are invaluable eyes and ears in a hospital setting."

The recent changes to the internal medicine training shortlisting criteria, in which the leadership domain was removed, are therefore jarring. This might discourage future applicants from gaining leadership experience and could have an ongoing effect on the workforce.

Alice McGalliard, foundation year 2 doctor, Belfast

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Additional opportunities and resources

The Healthcare Leadership Academy (HLA)'s scholars programme is a year long, funded leadership development programme mapped to the NHS leadership framework that nurtures and empowers tomorrow's healthcare leaders. The programme can be undertaken in parallel to studies or work and explores the leader as communicator, manager, follower, negotiator, philosopher, and entrepreneur.

Peer learning and mentorship are core to the programme, with past scholars acting as organisers, mentors, and cohort directors. For us, a key benefit is the diversity of scholars that we learn with and from. Scholars come from a wide range of professional backgrounds, career stages, and countries.

In addition, the Faculty of Medical Leadership and Management offers some free online resources. These include "how to" guides (such as *How to Chair a Meeting*); a repository of leadership opportunities curated by region; and the Leadership Development Passport, a document in which to record evidence and map progress to recognised standards.

Christopher J Graham, digital education manager, Royal College of Physicians of Edinburgh; Laura (Josie) Cheetham, GP, Hereford

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DOCTORS IN LEADERSHIP ROLES

Training is essential

I agree with Oliver that attacking doctors who take up leadership roles is unhelpful, but we must explore why this happens (David Oliver, 26 October). There is a perception of a "clinician versus manager" atmosphere in the NHS.

Like any skill, leadership and management requires training to be effective. We cannot assume that a clinician automatically makes a good leader or manager.

Programmes are designed specifically for clinicians to develop leadership and management skills. The Cleveland Clinic is one of the best healthcare institutions in the world, and much of this is down to its leadership, made up of clinicians who undergo in-house leadership training leading to tangible benefits for patients and staff alike.

Leadership and management development should start at medical school and be part of every postgraduate curriculum. I can think of no other industry where leaders or managers are appointed without training.

Kwaku W Baryeh, North West London international medical graduate education fellow, Isleworth

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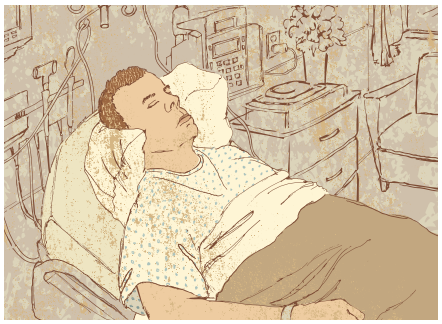
WHAT'S IT LIKE TO BE A PATIENT AS A DOCTOR?

Both ends of the stethoscope

Best writes about doctors becoming patients (Healthcare for Doctors, 19 October). My inventory of ailments is well into double figures—I thought that getting old would take longer.

Everyone, patient and doctor, is unique. Doctors as patients can present different challenges to the general population, can find the patient role an unwelcome novelty, and can elicit unanticipated responses from the doctor they consult. Differences between professional generations—knowledge, consultation style, bureaucratic burden, corporatist environment—can also complicate matters.

Medicine will always be a demanding and complex profession. My intuition is that the complexity, the exponential growth of knowledge and investigative or therapeutic options, the endless corporatist intrusion, the relentlessly malcontent media, and political perversity might combine to make



coherent and effective healthcare very nearly or actually impossible.

We can use our personal experiences, from both ends of the stethoscope, to inform future developments. Is there scope for research in this direction?

Steven Ford, retired GP, Haydon Bridge

Cite this as: *BMJ* 2024;387:q2555

Colleague patients might be right

Good communication skills are particularly important when dealing with doctors as patients, but I am a little concerned about the emphasis on not being "manipulated into doing something you wouldn't normally do."

When doctors are consulting about a potentially serious illness, they should be able, having explored the patient's ideas and concerns, to agree on the actions necessary. But if there is a difference in opinion with an experienced colleague, then it is important to consider that the patient might be correct.

Clinicians often have a clinical hunch that something is wrong and might have experienced that this can be worth listening to. Doctors should be sensitive to the specific worries of colleague patients and to recognise when these have not been fully dealt with. In this situation, a senior second opinion can be very helpful rather than a dogmatic refusal to be bullied.

Phil Taylor, retired GP, Axminster

Cite this as: *BMJ* 2024;387:q2561

MEDICAL APPRENTICESHIPS

Much better than passive clinical placements

Lynn's summary of medical apprenticeship made us reflect on our own experiences through medical school (Cover, 13 January). We would have loved the opportunity to be apprentices.

Notwithstanding the advantageous financial circumstances of avoiding hundreds of thousands of pounds of debt, the medical apprenticeship programme offers apprentices the opportunity to become legitimate participants in communities of practice in a way that passive clinical placements do not.

The apprentice will initially undertake administrative duties, such as working as ward clerks or porters. The paid component could include assisting in the phlebotomy service or being part of the vascular access team.

Clinical placements were suspended during the covid-19 pandemic, leading to medical students like us undertaking paid clinical duties in vaccination centres or as medical technicians. Those involved said that paid multidisciplinary work positively affected their professional identity as a future doctor, in a way not currently achieved by passive clinical placements.

John Gillespie, foundation doctor; Antony Fernando, foundation doctor; Hozafa Ali, foundation doctor, London

Cite this as: *BMJ* 2024;387:q2571

ENDOMETRIOSIS CARE

Reasons for cautious optimism

I agree with Mahase that many challenges exist in endometriosis diagnosis and management, but there has been some progress (This Week, 20 July).

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists has created guidelines for diagnosis and management of endometriosis. The National Endometriosis Clinical and Scientific Trials Network registry was established in 2018, encouraging collaborative research between clinicians, allied healthcare providers, researchers, and endometriosis advocates. Although it will take time to see the fruits of these collaborative efforts, these initiatives are important steps towards improving the diagnosis and management of endometriosis in Australia.

Laboratory and clinical advances are also being made. One recent study used microRNA biomarkers to non-invasively diagnose endometriosis; another used protein biomarkers for diagnosis and differentiating between different stages of endometriosis. Emerging pain treatments include hormone manipulation or suppression and esketamine infusion. Despite the challenges that remain, there is cause for cautious optimism.

Ayesha Hooda, master of public health student, Fitzroy

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HARD TO SWALLOW GUIDELINES

We can't ignore evidence based medicine

Guidelines are not only hard to swallow but impossible to use (John Launer, 19 October).

Most guidelines are for single conditions, but most patients over 60 have a multiplicity of conditions. Were we to "follow the guidelines," we would undoubtedly transgress the basic Hippocratic principle of "first, do no harm" in attempting to do the perceived best for the patient.

In their slavish adherence to guidelines, clinicians ignore the precept of evidence based medicine, which is distilling the evidence and applying it judiciously to the needs of the individual patient.

The incorporation of real world evidence into guidelines has the potential to complement knowledge gained from randomised controlled trials and is being actively pursued in some quarters as a legitimate strategy.

Naturally, any guideline needs to encompass not only the cost of delivery but also the benefits to society from health and economic gains, which might be greater than the costs incurred.

Dermot Ryan, retired GP, Kegworth

Cite this as: *BMJ* 2024;387:q2573

OBITUARIES

David Samuel Hopton

Consultant surgeon (b 1934; q Manchester 1958; FRCS), died of old age on 6 February 2024

David was born in Sale and attended Calday Grange Grammar School, then Sale County Grammar School. Following medical school and house jobs, he spent two years in national service. This was followed by attachments to the 2nd Battalion Parachute Regiment and the Special Air Service. He demonstrated anatomy in Edinburgh and held posts in Oxford, Preston, Manchester, and south Wales. A year of research in Seattle led to a consultant post in York. David took a lead clinical role in the planning and delivery of the new district hospital in 1976 and helped advance breast cancer services. In retirement he enjoyed sailing and tennis, and became a trustee for the Leonard Cheshire Foundation and several local charities. He leaves Janet, his wife of 60 years; three children; and nine grandchildren.

Barny Hopton

Cite this as: *BMJ* 2024;387:q2520

Olumade Adetola Okubadejo

Consultant microbiologist (b 1928; q London 1958; FRCPath), died from frailty of old age on 31 August 2024

Made Okubadejo was born in Lagos, Nigeria. He worked as a teacher and a clerk in the Nigerian government before coming to the UK to take his A levels. He then studied medicine at King's College London. He married Fay, a trainee teacher, in 1958. Made decided to pursue pathology and was appointed a registrar at Hammersmith Hospital. He returned to Nigeria and completed a doctoral thesis. In 1971 Made returned to the UK to take up a post as a consultant microbiologist in Portsmouth, becoming director of the public health laboratory in 1983. He was also the medical registrar at the local crematorium and an honorary lecturer at Southampton University. Made had a strong Christian faith and was a dedicated family man. Made is survived by Fay; three children; and five grandchildren.

Deyo Okubadejo

Cite this as: *BMJ* 2024;387:q2527

Emma Margaret Ellen Ahlqvist

GP (b 1982; q Dundee 2007), died from an intracranial haemorrhage on 7 July 2024

Emma Ahlqvist (née Rankin) was born in Belfast in 1982. From 2001 to 2007 she lit up Dundee Medical School and she then joined the GP training programme in Edinburgh. Once a GP she saw the challenges that the frail elderly population faced. In the Hospital at Home service, Emma navigated end of life care discussions with sensitivity. She was also quality lead for East Lothian primary care. Throughout her career she took the opportunity to educate students and team members. In 2022 Emma was awarded a place on the Scottish Quality and Safety Fellowship programme. The passion that Emma brought to her work shone through her wider life. Emma loved travel, art and fashion, yoga and dance, and family and friendship. She leaves her husband, Jacob; sons Thomas and Philip; and her mum, Linda.

Jacob Ahlqvist, Catherine Macklon

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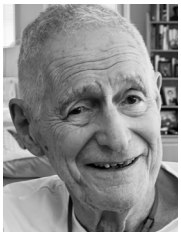
Godfrey David Ripley



Family physician and academic (b 1930; q London 1953; FAAFP), died of effects of cerebral stroke on 29 October 2024

Godfrey Ripley was born in London and after graduating trained in analytic psychotherapy at the Tavistock Clinic, London. He interned at Hackney Hospital and entered general practice with his GP father in north west London. After a stint in Jamaica Godfrey and his young family returned to the UK and he joined a practice in Elstree and Borehamwood, Hertfordshire. In the late 1960s he was recruited to the US, serving at Duke University and the University of Connecticut. He was on the faculty of the American Institute of Medical Education, contributing regular presentations at many of the institute's Creativity and Madness conferences, which continued through his retirement. He is survived by his second wife, Anna-Lena Helmer; three children; four grandsons; and four great grandchildren.

Jim Ripley, Sally Ripley

Cite this as: *BMJ* 2024;387:q2525

Charles Shaw

Independent consultant for quality in healthcare (b 1944; q 1969 London; FFPH, FIHCM), died from prostate cancer on 12 December 2023

Charles was born in London and was brought up in an artistic family. He trained as a physician at Middlesex Hospital and after a variety of posts he spent six years as medical director of the King Edward VII Memorial Hospital in Bermuda. Here he was exposed to new ideas, such as standards and clinical audits. This led to his doctorate in 1986 from the University of Wales. Charles became an expert in quality assurance, advising the World Health Organization, World Bank, and universities globally. He wrote a book and edited and wrote numerous papers. Charles was a devoted family man. He loved music, the *Times* crossword, and good food and wine, as well as pursuing his academic interest in research and analysis—of almost anything. He is survived by Carolyn, their children, and two granddaughters.

Mike Toynbee

Cite this as: *BMJ* 2024;387:q2523

Vinit Sheshnath Vedpathak

Anaesthetist (b 1956; q Mumbai 1981), died of myocardial infarction on 12 September 2024

Vinit was born in Mumbai, India. He graduated from the Maharashtra University of Health Sciences in 1981 and came to the UK in 1989. After working in Dover, Lincoln, and Birmingham he settled in north Wales and Chester, serving the communities of Bodelwyddan and Wrexham. Vinit was a respected mentor known for his expertise and dedication to teaching practical anaesthetic skills. Vinit married Nutan in 1983 and together they raised two children: daughter Shreya, a dental surgeon, and son Omkar, a software specialist. Vinit was a proud family man. His love and commitment extended beyond his immediate family; he was a lively member of his community, often hosting local gatherings. He retained his smile and optimism until the end. He leaves Nutan; Shreya and Omkar; and two grandchildren.

Omkar Vedpathak, Shreya Kumar, Nutan Vedpathak, Nikhil Kaushik

Cite this as: *BMJ* 2024;387:q2519

Michael Scallan

Anaesthetist whose career spanned the early days of paediatric heart surgery

Michael John Herbert Scallan (b 6 September 1943; q1967 Cape Town), died from pneumonia and complications of Parkinson's disease on 19 April 2024

Michael Scallan was sailing his first ocean passage on a leg of the 1999 Clipper Round the World yacht race when the navigation system failed in the middle of the Indian Ocean. As one of only two crew members able to navigate by the stars, he dusted off the yacht's sextant and set the boat back on course. "To our surprise and delight we obtained a noon latitude within one to two miles of the GPS reading," he recalled.

This ability to adapt to the vicissitudes of life was equally evident in the operating theatre, where one colleague remembered him as "calm and serene but always quietly engaged with the procedure in hand." Another described him as "totally in control of whatever situation transpired, unfailingly supportive whenever an operation proved to be unusually challenging."

Paediatric congenital heart surgery was still novel when Scallan joined the Royal Brompton Hospital in London as a consultant anaesthetist in 1977. In the early days his work included paediatric intensive care, a specialty that was only just emerging. He and his colleagues were soon taking referrals from across Britain and overseas, and he remained at the forefront of the field for 40 years.

Awed at his ability

Scallan was one of the earliest anaesthetists to facilitate the primary correction of congenital heart defects in infants and neonates, working with surgeon Christopher Lincoln and cardiologist Elliot Shinebourne to develop improvements in cardiopulmonary bypass in children. He was also the first anaesthetist at the Brompton to support surgery for hypoplastic left heart syndrome. Colleagues were awed by his ability to insert multiple central lines in sick children, in the days before modern multi-lumen lines.

With the decline in child mortality following surgery for congenital heart disease, attention increasingly focused on morbidity, particularly neurological morbidity. Scallan, who contributed to more than two dozen journal articles, insisted that "prevention and treatment must start during the preoperative period and continue through the intra and postoperative periods."

Scallan was always 'totally in control' of whatever situation transpired

Michael Scallan was born in Cape Town, South Africa, the second of three children of Desmond Scallan, an Irish born civil servant, and his wife Cherry (née Ramsey), a theatre sister who had trained in London. He grew up with a love of the sea and surfing, and would reminisce fondly about road trips through Botswana, Mozambique, and Zimbabwe.

Although he took his medical studies at the University of Cape Town seriously, friends also remember him as a committed poker player. One recalled that he was never on the losing side, adding, "He was just too smart for us all."

His distaste for South Africa's policy of apartheid meant he was reluctant when called up for national service—his mischievous side soon made an appearance, however. While on exercise in Port Elizabeth he was tasked with driving the army's newest Land Rover to Grahamstown (now Makhanda) in the Eastern Cape, a journey of about 150 km (93 miles). Such was the value placed on this addition to the fleet that he was instructed to drive slowly and carefully. Dutifully following orders, he completed the journey in three days, having squeezed in a tour of the province.

His pessimism about South Africa's future led to his using his Irish passport to leave the country in the 1970s, first for Nijmegen in the Netherlands and then London, where he was appointed to a training post at Northwick Park Hospital in Harrow before joining the Brompton. He was a patient teacher, allowing trainees to take responsibility for their own actions while knowing when to intervene to avoid disaster.

Scallan, who also worked privately at the Wellington Hospital and the Harley Street Clinic, retired in 2007. He lived close to Lord's cricket ground, which he enjoyed visiting with family and colleagues. He was also passionate about skiing. His son Nick recalled being caught with him in a storm on the mountains of Anzère, Switzerland. Visibility was only a couple of metres, snow was biting any sliver of exposed skin, and their hair was frozen into icicles. Refusing to panic, Scallan slowly and methodically led his son down the mountain to safety.

Humour in adversity

His ability to meet adversity with humour combined effortlessly with a nuanced understanding of how the world works. On one occasion he was visiting South Africa with Nick, who was conned into handing over £10 to an official looking baggage assistant. He told his son that he had "paid what he felt to be the going rate."

Scallan briefly came to public attention in 2018 after Kamal Al-Hirsi, a cleaner at Bannatyne's health club in Maida Vale, was found unresponsive in the swimming pool. The inquest heard how during resuscitation efforts Scallan, who was in the club that day, checked Al-Hirsi's pupils but found them "fixed and dilated."

He was married to Gillian (née Hedges) for 35 years; their first date was a performance of Puccini's *La Bohème*. Gillian introduced him to sailing, and he competed in the Sydney-Hobart and Fastnet races, as well as the Clipper Round the World race.

He is survived by Gillian; his siblings, Margaret and Brian; his children with Gillian, Ed and Nick, who followed him into anaesthesia; and by his children from an earlier marriage, John, Andrew, David, and Morwenna.

Tim Bullamore, Edinburgh
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