comment

"Many comments on the Tavistock have been partisan and ill informed" **JOHN LAUNER**
"Am I out of step with my peers or are NICE guidelines unrealistic?" **HELEN SALISBURY**
PLUS Diversity in the public health workforce; the scrutiny of Hancock

THE BOTTOM LINE Partha Kar

Antiracism starts with an apology

The stream of depressing, hurtful stories about treatment of NHS employees has been relentless. We're left to wonder whether we've reached a tipping point or whether we'll have to hear about more suffering before the NHS takes action beyond platitudes, hashtags, or faux outrage.

This month an NHS midwife, Olukemi Akinmeji, successfully sued the NHS trust that had employed her from 2018 to 2020 for race discrimination. Last month NHS England lost an employment tribunal case against Michelle Cox, a senior nurse, on grounds of race discrimination and whistleblowing. Also this month Valentine Udoye, a doctor who had been cleared by a medical practitioners tribunal of any misconduct, had to face a new tribunal after the General Medical Council appealed the case in the High Court, and he went on to win the new tribunal case. Last August the *Times* covered the case of Melissa Thermidor, who lodged an employment tribunal claim against NHS Blood and Transplant saying that she'd been constructively dismissed after whistleblowing about racism in the organisation.

A common thread runs through these stories: they're all about individuals from the black community. And they're no longer isolated events. New GMC data on differential attainment among trainees show that being black affects attainment negatively. In response, without fail, the old chestnut of "Ah, but it's linked with deprivation" comes up. And yet this data analysis has one stark fact: the richest black individual has a poorer outcome than their poorest white colleague. These data are all for UK graduates—same schools, same exams, same educators, same assessors.

Yet, even with such stark data points and tribunal outcomes, there's little accountability for these failings. We don't need more data or "granularity" to highlight the problem. We just need data to track progress on dealing with these failings and to hold to the fire the feet of those whose job it is to tackle inequalities but have done nothing.

There are many things we could do, and the researcher Roger Kline has eloquently stated the role that HR teams should play. But we also need more fundamental change, and that starts with an apology.

This is the 75th anniversary of the Windrush generation, and there has to be a point when someone stands up and says the keyword: sorry. Acknowledge we as a health system have failed people from the black community, whether in their health outcomes, careers, or the way black health workers are treated. Nothing suggests that in 2023 they're treated on a par with their colleagues, and yet we fail to acknowledge this in public.

Let's be honest: if we know the data and we haven't done all possible to bring equity to fellow human beings, and we judge them on the basis of skin colour, what term should we use for ourselves but racists?

Partha Kar, consultant in diabetes and endocrinology, Portsmouth Hospitals NHS Trust drparthakar@gmail.com
Twitter @parthaskar
Cite this as: *BMJ* 2023;380:p534

We have to acknowledge that we as a health system have failed people from the black community

OPINION Kazim Beebeejaun and Kerry Littleford

Diversity in the public health workforce is key to its success

Lessons from the pandemic can prepare us for future challenges

The pandemic provided an opportunity to learn and rethink what a well equipped public health workforce looks like. To tackle health inequalities meaningfully and build long term trust with the UK's deprived communities, we must first confront inequities and biases in our own profession.

At its core, public health promotes broad, multidisciplinary thinking about health, examining structures and barriers that influence unjust and avoidable differences in people's health. Covid-19 exposed and exacerbated longstanding health inequalities in our society. Communities living in the most deprived areas and ethnic minorities were up to twice as likely to die from the virus and had higher levels of vaccine hesitancy and distrust of government.

The pandemic presented many stark lessons for public health in terms of preparing for the inevitable next pandemic. However, evidence is growing that the public health workforce does not always represent the populations it serves, prompting the question—how ready is our system to act on these lessons and to meaningfully engage with the population?

The UK Faculty of Public Health has been proactive in addressing diversity in the public health workforce by commissioning an investigation into differential attainment in training, with a recent report showing stark differences in the success rates of certain groups. Black candidates were 90% less likely to be successfully appointed to the UK's primary training programme than white candidates. Asian candidates were 30% less likely.

Greatest disparities

Differential attainment by ethnicity in medical specialty programmes is nothing new. Thirty years ago, research showed that doctors with English names were twice as likely to be successfully appointed to medical specialties as those with Asian names, despite having the same professional backgrounds. In 2020, a report using GMC data found that public health had the greatest disparities of all 14 medical specialties, with one in seven ethnic minority candidates appointed, compared with more than one in three white candidates.

Questions remain over mistakes made in response to covid-19 and implications for how to prepare for future pandemics. For instance, a key theme at the UK Health Security Agency conference in October was how to tackle the health inequalities exposed by the pandemic.

Building trust requires consistency in our values as a profession

Plenary panels of senior public health leaders discussed the importance of building trust in communities at all times, not just in emergencies.

Putting aside issues of equity and fairness in recruitment, we argue three reasons why greater diversity in the public health workforce is needed to act on the pandemic's lessons. First, cultural competence is essential in gaining a rich understanding of the perspectives, needs, and concerns of marginalised communities. Complex sociocultural and historical factors interact to influence views of healthcare. For example, vaccine hesitancy in black communities is heavily influenced by historical mistrust of government and medicine linked to British colonialism and unethical experimentation.

Cultural competence rooted in experience is a powerful tool for positive change. Public health messages from trusted sources within communities help increase confidence, trust, knowledge, and acceptance of interventions. Professionals cannot become culturally competent by reading academic sources alone. A workforce with real world experiences is key to tackling the challenges ahead.

OPINION Gareth Iacobucci

Scrutiny of Hancock's handling of the pandemic is far from over

The erstwhile health secretary turned reality TV "star" Matt Hancock is back in the headlines.

On Sunday 26 February, Hancock was asked to explain why he appeared to be wearing a signed Newcastle United shirt that he had previously auctioned off to raise money for charity. A Magpies fan since his "Geordie Uncle Dave" used to take him to games when he was young, Hancock had posted a TikTok video (of course he's on TikTok) wearing the shirt shortly before his team lost to Manchester United in the Carabao Cup final. In a swift clarification on his choice of garment he explained he had sold the shirt but that it was gifted back to him by the person who had bought it. So, aside from his team losing, there wasn't too much harm done.

These messages show the discourse when policy decisions were made

But things took a definite turn for the worse for Hancock on the morning of 1 March when the *Daily Telegraph* published details of 100 000 WhatsApp messages that he had exchanged with ministers and officials during the pandemic. The most damaging claim from the messages is that, when he was health secretary, Hancock had dismissed expert advice from Chris Whitty, England's chief medical officer, to test anyone going into a care home—from hospital or the community—for covid at the start of the pandemic.

Isabel Oakeshott—a prominent lockdown sceptic—obtained the messages while working on *Pandemic Diaries*, Hancock's memoir, which she ghostwrote last year. Her decision to release them to the newspaper has angered Hancock, who immediately responded saying the private messages were "stolen" and the interpretation of them was "categorically untrue." Oakeshott's justification was that it would take many years to conclude the official covid public inquiry, which she claimed was at risk of being a "colossal whitewash."

Second, a more diverse workforce is more innovative. Covid-19 exposed gaps in our thinking at a systemic level. A growing body of private sector evidence illustrates the benefits of diversity. For example, a recent large meta-analysis of more than 170 companies found that those which were more diverse had higher levels of revenue from innovative services and products. Similarly, psychological studies have found that experiences of diversity challenge our ways of thinking, driving innovation in ways that homogeneity cannot.

Third and most importantly, building trust requires consistency in our values as a profession. We cannot advocate for equity and social justice in health without tackling inequalities within our own community.

How prepared we are for the next pandemic and how well we adapt to the lessons learnt from covid-19 will be a key challenge. However, we will not make meaningful progress without first reducing the inequity in our profession.

Kazim Beebeejaun, specialty registrar in public health, co-chair

Kerry Littleford, specialty registrar in public health, NHS, co-chair Faculty of Public Health Equality and Diversity Special Interest Group

Cite this as: *BMJ* 2023;380:p447

There was further embarrassment for Hancock on Thursday when it emerged he had described teaching unions as "absolute arses" during an exchange with the then education secretary Gavin Williamson over the decision to delay A level exams because of covid.

Quite apart from what these messages show us about the standard of discourse in government when major policy decisions were being made, the key lesson for Hancock here is to choose your ghostwriter very carefully. With further leaks expected, and with preliminary hearings of the covid-19 public inquiry kicking off this week, his transition from Westminster to light entertainment after his controversial appearance on *I'm a Celebrity…Get Me Out of Here* seems unlikely to be as black and white as his beloved Newcastle United shirt.

Gareth Iacobucci, *The BMJ*

Cite this as: *BMJ* 2023;380:p516

TALKING POINT John Launer

Gender, polemics, and empathy

I worked part time for many years at the Tavistock Clinic in London and still hold an honorary post there. The clinic is one of the most prestigious teaching institutions for psychological treatment in the NHS and the world. I'm proud to be associated with it.

My role was in primary care education and as a family therapist. I never worked with patients who had gender dysphoria, although I was aware of a small unit there that specialised in helping them. The unit has figured much in the news recently.

Over my years at the Tavistock I got to know several colleagues who worked in that unit. I heard how the numbers of young people they saw rose exponentially, in line with social awareness of gender dysphoria and public acceptance of it. They often dealt with hostility from patients, families, and pressure groups who believed the service should offer treatment more readily. Internally, they faced criticism by some clinicians who believed in a more cautious approach involving a much longer assessment. I knew and respected people who held passionate positions on both sides of this question.

The stresses on the service continued to increase, and the debate about approaches eventually erupted in a very public controversy. This was played out with the involvement of the courts, the Care Quality Commission, and the media. It culminated last summer with an interim report from Hilary Cass, a former president of the Royal College of Paediatrics and Child Health, that recommended the closure of the service and its replacement within specialist children's hospitals. This was widely reported in the national press and *The BMJ*.

Since then I've been concerned to hear, overhear, and read a lot of angry or critical words about the affair. Many comments have been partisan and ill informed, including false reports that the entire Tavistock Clinic was shutting down. Few people offering their views with vehemence and certainty seem to have read the Cass report itself, which is even handed and nuanced, looking at the wider historical and cultural contexts in which problems have developed.

It is worth trying to understand, as Cass did, the predicaments faced by everyone involved. There were young people who desperately wished to change their gender but found that medical and psychological support in the UK was massively lacking. Some patients underwent gender change but uncovered other psychological conflicts for which support was also deficient. Some clinicians strove to make the best decisions they could in a situation where evidence was thin and the politics noisy. Those who believed in a prolonged therapeutic approach didn't have the resources to offer this either. It's not clear whether these will be available in the new services.

Cass wrote in her report, "As with many contemporary polarised disagreements, the situation is exacerbated when there is no space to have open, non-judgmental discussions about these differing perspectives." What we need most now are empathy and dialogue, not polemics and blame.

John Launer, GP educator and writer, London

Cite this as: *BMJ* 2023;380:p477

Few people offering their views with vehemence seem to have read the Cass report

PRIMARY COLOUR Helen Salisbury

Benchmarking and ideal guidelines

In their personal statements, medical school candidates often wax lyrical about embarking on a journey of lifelong learning in the ever changing worlds of science and medicine.

These days I admit my journal reading is scant, and the internet provides most of the information that keeps me abreast of change. It answers many of the questions that arise in daily practice—the known unknowns—and can do this in real time, often in the consultation. Alongside this—and revealing the unknown unknowns—I attend an annual update course.

At these courses the lecturers have five hours to try to cram in the most significant changes to the NICE guidelines that are relevant to GPs. Pre-covid, attending this course was always an enjoyable event, doubling as an opportunity to catch up with local colleagues; unfortunately, I had to attend the latest iteration remotely. There are good "green" reasons for remote learning, as well as reducing the risk of covid transmission, but it comes with significant disadvantages, not least the difficulty I have staying focused on my laptop for five hours. But the biggest loss for me is that of the opportunity to benchmark.

Sometimes, when recommendations are presented, I feel content that my practice is roughly in line with the guidelines. Quite often, however, I'm aware that my usual way of working is very different from the "gold standard" being presented. When this happens, what I really need to know is whether I'm out of step with my peers or whether it's the guidelines that are unrealistic. Listening to a presentation in a shared auditorium, you rapidly get a sense of whether the information is new or surprising to most and whether there's a general feeling of acceptance or dissent.

This year the latest guidelines for treating depression were presented. These included the menu of modalities of treatment we should be offering: 11 options for milder depression and 10 for more severe depression. I think we were probably all muttering "in your dreams" under our breath but, attending remotely, I couldn't tell. The suggestions about what should be covered in each consultation seemed predicated on a very much longer meeting than the average GP appointment and included the recommendation that all patients who start medication for depression should be given personalised written information fully explaining the harms, benefits, and risk of withdrawal.

I'd be interested to know if some practices feel able to offer the care in these guidelines. Clearly, they're aspirational and directed partly at commissioners, given they suggest a range of treatments not widely available—but they reveal a yawning gap between the ideal as imagined by NICE and the reality in the land of primary care.

I wish I'd been sitting with colleagues and been able to find out whether I was alone in my response. As it is, I'm not sure if—or how—I'll alter my practice.

Helen Salisbury, GP, Oxford
helen.salisbury@phc.ox.ac.uk
Twitter @HelenRSalisbury

Cite this as: *BMJ* 2023;380:p532

There's a yawning gap between the ideal as imagined by NICE and the reality in the land of primary care

LATEST PODCAST

Being yourself at work

How much should doctors share with patients about their identity or personal life? This episode of the Sharp Scratch podcast features guest Brendan J Dunlop, a clinical psychologist, who talks about the ways in which self-disclosure can strengthen relationships and care:

"In medicine your patients have got to trust you and they've got to feel like you are people they can talk to. We work in roles that often emphasise power differences. If we can have conversations that break down that power, which sharing things about ourselves can sometimes do, I think that's really important."

Yet Dunlop also points out that these acts of disclosure may not always be within a doctor's comfort zone or even control:

"Disclosure is often not a choice for people. So if somebody is visibly pregnant, for example, or that's the assumption we make about them, they have told us something about their lives that we haven't had to ask about. Race and ethnicity is also a visible disclosure that you haven't got any control over and which can invite conversation or assumptions."

Sharp Scratch panellist Maz Sadler, a final year medical student, shares how this echoes some of her experiences:

"I was pregnant on placement last year and I got the full gamut of questions and comments. For some reason, pregnancy seems to be something that everybody is entirely comfortable asking you about or making judgments about. Some of the things that people felt comfortable saying to me were unbelievable. I think it would be really valuable for anybody who has patient interactions to sit down and think what can I say when I want to shut down a conversation without it being rude? There were some times when I was pregnant when I wished I had the vocabulary to do that."

Listen and subscribe to *The BMJ* podcast on Apple Podcasts, Spotify, and other major podcast apps

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

ANALYSIS

Replacing RCTs with real world data for drug approval: a self-fulfilling prophecy?

Absent data from randomised controlled trials, increasing use of real world data to approve new medicines is the wrong remedy for challenges in drug development, argue **Beate Wieseler and colleagues**

Attempts to accelerate the provision of new treatments have led to evidence that is limited in quantity and quality being submitted for regulatory approval in recent years.[1 2] Approvals based on single arm trials, for example, have become more frequent, such as for lisocabtagene maraleucel, a CAR-T cell therapy for patients with B cell lymphoma. Single arm trials are not informative enough to enable us to select the best therapy for a patient among several options.

This lack of robust evidence—especially the lack of comparisons with standard care—has implications for decision making in clinical practice and health policy, as the place of new drugs in the treatment landscape remains unclear, and reimbursement and pricing decisions cannot be adequately informed.[3 4]

Current discussions of the most suitable study types for regulatory approval and the question of whether observational data instead of data from randomised controlled trials (RCTs) would suffice are relevant beyond regulatory agencies.[5 6] The question is intertwined with the potential use of routine practice data, often referred to as real world data or real world evidence (box 1). The debate about these data started in the United States with the Food and Drug Administration's framework for a real world evidence programme.[7] The European Medicines Agency (EMA) followed with a series of articles but suggested different evidence sources be used for the collection of real world data. In contrast to the FDA, the EMA seems to exclude RCTs from its use of routine practice data.

The EMA outlined its approach to introducing real world data into regulatory decision making in a recent series of papers.[8-11] So far, it largely uses real world data to inform decisions on safety,[12] thus confirming that "their evidentiary value, notably for demonstrating efficacy, requires further evaluation."[11] Nevertheless, the EMA predicts that "by 2025 the use of real world evidence will have been enabled, and the value will have been established across the spectrum of regulatory use cases."[11]

KEY MESSAGES

- Enthusiasm is growing for the use of observational real world data as a basis for regulatory, clinical, and health policy decision making
- Observational, non-randomised study designs are ill suited to measure the treatment effects of new drugs
- Promoting the use of observational studies from routine practice data sources might hinder efforts needed to improve the feasibility of RCTs
- To ensure high quality and efficient healthcare, the conduct of RCTs should be made easier, faster, and cheaper

Box 1 | Definitions of real world data

US Food and Drug Administration (FDA)

The FDA defines real world data as "data relating to patient health status and/or the delivery of healthcare routinely collected from a variety of sources," not restricting study designs. It defines real world evidence as "the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of [real world data]," which can be generated using different study designs "including, but not limited to, randomised trials (eg, large simple trials, pragmatic trials), and observational studies (prospective or retrospective)."[7]

European Medicines Agency (EMA)

The EMA defines real world data as "routinely collected data relating to a patient's health status or the delivery of healthcare from a variety of sources other than traditional clinical trials,"[8] thus restricting the study designs that can be used to generate real world data. The EMA has published inconsistent information on this restriction of study designs—it previously noted that data from pragmatic (randomised) trials would be included if collected under conditions of normal clinical care, citing the randomised Salford Lung Study as an example.[8]

But, in a more recent publication, real world data and evidence seem to be restricted to non-interventional preauthorisation or postauthorisation studies or sources other than RCTs.[9] The Data Analysis and Real World Interrogation Network (DARWIN EU), the EMA's main tool for the provision of real world data, is also limited to observational data sources and non-interventional studies.[10]

The lack of clarity in definitions is hampering discussions about real world data use, especially for the main question in regulatory decision making: the evaluation of effects of new interventions. The difference between the FDA and EMA with regard to the inclusion of interventional, randomised studies is of major importance.

The option to collect additional data on a new drug's benefits and harms in routine practice has been an integral part of accelerated approvals based on limited evidence. More recently, the increasing availability of large datasets from electronic sources—such as electronic health records, medical claims data, and patient registries—has fuelled the debate about using real world data for determining treatment effects of new drugs, even beyond accelerated approvals.[13 14] Scientists from the EMA, the EMA's Committee for Orphan Medicinal Products, and the Danish Medicines Agency,[6] as well as industry associated authors,[15] say that drug development based on RCTs is becoming more and more difficult owing to factors such as the growing number of drugs for rare diseases, very small subpopulations, individualised treatments, and patient preferences.

We argue that the current European focus on generating evidence for decision making in healthcare using observational real world data, and thus potentially replacing RCTs, is the wrong remedy for the challenges in drug development.

Pivotal studies in approvals of treatments for relapsed or refractory diffuse large B cell lymphoma

	Pixantrone	Tisagenlecleucel	Axicabtagene ciloleucel	Polatuzumab vedotin	Tafasitamab	Lisocabtagene maraleucel	
Brand name	Pixuvri	Kymriah	Yescarta	Polivy	Minjuvi	Breyanzi	
Date of first approval	May 2012 conditional approval	Aug 2018 standard approval	Aug 2018 standard approval	Jan 2020 conditional approval	Aug 2021 conditional approval	Apr 2022 standard approval	
Indication	≥2 previous treatments	≥2 previous treatments	≥2 previous treatments	≥1 previous treatment, SCT ineligible	≥1 prior treatment, ASCT ineligible	≥2 prior treatments	
Orphan designation	no	yes	yes	yes	yes	no (withdrawn)	
ATMP	no	yes	yes	no	no	yes	
Pivotal studies	PIX301*RCT (phase 3)	C2201single arm (phase 2)	ZUMA 1 single arm (phase 1/2)	GO29365RCT (phase 1b/2)	L-MIND single arm (phase 2)	017001 single arm (phase 1)	BCM-001single arm (phase 2)
Comparator arm	yes	no	no	yes	no	no	no
No. of patients enrolled in treatment arms	Pixantrone 70 (53 with DLBCL); Physician's choice 70 (51 with DLBCL)	147	111 (77 treated for DLBCL)	Polatuzumab+BR 40; BR 40	81	341	58
Primary endpoint	CR	ORR	ORR	CR	ORR	safety and ORR	ORR

*aggressive NHL including DLBCL. ASCT, autologous stem cell transplantation; ATMP, advanced therapy medicinal product; BR, bendamustine/rituximab; CR, complete response; NHL: non-Hodgkin lymphoma; ORR, objective response rate; RCT, randomised controlled trial; DLBCL: diffuse large B cell lymphoma, SCT: stem cell transplantation.

When to use real world data

Real world data can be useful to investigate, for example, the size and characteristics of a specific patient group of interest, over longer time periods, or to describe the current standard of care in a patient population. These uses are not the focus of this article. Here we focus on whether real world data can be trusted to reliably measure treatment effects of new drugs—health outcomes causally related to treatment.

The challenges of measuring treatment effects of interventions in observational, non-randomised studies have been discussed for decades.[16] The main one—being sufficiently certain about whether a difference in health outcomes between patient groups receiving different treatments is related to the treatment or merely to differences in patient characteristics—is still largely unsolved. In addition to unknown confounders, there is the question of whether real world data sources would include the information required (both in quantity and quality) to adjust for differences in known confounders.

Suitability of real world data for regulatory decision making

Studies on whether observational real world data are suitable for investigating treatment effects use different approaches. One approach is to compare the treatment effects derived from RCTs with those from observational datasets, which has produced conflicting results.[17 18] A limitation of this approach is that any difference in effects between the two study types might reflect differences in patient characteristics or the application of interventions rather than tell us anything about the validity of observational studies. Regardless, these studies could neither show that real world data provide consistent effects (even when newer analysis methods were used) nor identify any study or disease characteristic that would be predictive of consistency and could thus help to decide in which cases regulators could rely on real world data.[17 19]

A second approach is to investigate the extent to which real world data sources include the information required to run the necessary analyses to adjust for potential differences between patient groups, thereby tackling the major obstacle of non-randomised studies. Indeed, the availability of reliable information on relevant outcomes—including mortality, clinical events, and patient reported outcomes (symptoms, health related quality of life)—in real world data sources has been analysed. The studies available have found substantial limitations around the required quantity and quality of data on confounders and outcomes.[20-22]

In the approval of advanced therapy medicinal products, the pivotal trials considered by the EMA were predominantly single arm studies

Similar findings have been reported for real world data in submissions to health technology assessment bodies; the comparability of patient populations receiving alternative treatment options could not be evaluated because data on patient characteristics were missing, raising doubts about the suitability of real world data for measuring the treatment effects of new drugs.[23]

Replacing RCTs: a choice rather than a necessity

The hypothesised infeasibility of RCTs is largely based on the assumption that they cannot be implemented in small populations. This might be true for specific "ultra-rare" diseases, but the generalisability of this argument is contradicted by findings from orphan drug development programmes. Analyses have shown that, in most cases, RCTs were actually available.[24 25] The German Institute for Quality and Efficiency in Health Care found that RCTs were available for about 60% of the new orphan drugs entering the German market between 2014 and 2018, with a wide overlap in the size of the target populations of the interventions between RCTs and observational studies.[25 26]

By contrast, in the approval of advanced therapy medicinal products (ATMPs)—that is gene therapies, somatic cell therapies, and tissue engineered products—the pivotal trials considered by the EMA were predominantly single arm studies.[28] These uncontrolled studies then required (non-randomised) external control arms for contextualisation. The rationale for primarily performing single arm trials is unclear, as the EMA recommends RCTs for ATMPs.[29]

An analysis of the feasibility of randomisation in approvals for treatments in relapsed or refractory diffuse large B cell lymphoma found that the pivotal trial was an RCT in two of six cases; the remaining four treatments (including three ATMPs) were approved based on one or two single arm studies (table). However, more patients were enrolled in the single arm studies than in the RCTs, so the assumption that randomisation is infeasible due to small patient populations is questionable, and the conduct of non-RCTs seems to be more of a choice than a necessity.

Information on treatment effects in clinical practice can be collected in pragmatic RCTs

A self-fulfilling prophecy?

Exceptional cases might exist in which RCTs cannot be conducted. But the narrative that RCTs are often infeasible while real world data are readily available could jeopardise the future conduct of RCTs, inadvertently reinforcing the idea they are not feasible. Their infeasibility could thus become a self-fulfilling prophecy. In the medium and long term, this could even hamper the development of new drugs and undermine the requirement for rigorous evidence of safety and effectiveness before allowing the widespread use of a new treatment.[30] Real world data should not be seen as the only or even the main option for tackling current challenges in drug development, especially not for determining treatment effects.

Beyond drug development, RCTs are also required for optimising the use of new interventions after approval, such as testing adjusted dosing or alternative treatment schedules for specific patient groups or exploring combination treatments. A narrative that questions the feasibility of RCTs would thus also affect this purpose. Given that patients can often only be included in one study, it seems efficient and ethical to enrol the small number of patients with a given indication in studies with the best possible study design.

Box 2 | Measures to enable RCTs in smaller populations

Improve study conduct, including patient recruitment

- Set up standardised patient registries for rare diseases and ensure data collection in routine care
- Set up a standardised trial infrastructure for studies in Europe and connect this infrastructure to networks outside Europe, as appropriate
- Identify patients for trials via patient registries[32]
- Conduct RCTs linked to information stored in patient registries[33]
- Use adaptive platform trials with master protocols across different treatment candidates[34]

Mitigate small patient numbers

- Avoid narrow inclusion criteria; include broader patient populations reflecting the target population
- Increase proportion of patients (for a given disease) in clinical trials
- Perform multinational trials (increasing and speeding up patient inclusion)[27]
- Use optimised study designs (such as adaptive designs) for trial efficiency[35]
- Use common control groups (through platform trials)[36]
- Apply statistical methods that tackle small patient numbers[35]

General

- Optimise study designs for decision making by both regulators and health technology assessment agencies to avoid the need for a larger number of trials[37]
- Involve patients in study design to ensure that the study conduct and information generated also meet their specific needs
- Maximise learning from studies (in small populations) by routinely making individual patient data available to the EMA and use the individual patient data available from the FDA for additional analyses (also across studies)[38 39]
- Accelerate clinical development by making new knowledge (including clinical study reports) publicly available as soon as possible[40]

Using the advantages of randomisation

If conducted appropriately, RCTs provide trustworthy estimates of treatment effects. But current RCTs are often overly complex, burdensome, and expensive. This limits the number of studies that can be performed to answer even the most urgent questions in healthcare. Methods to conduct leaner, less expensive RCTs (such as simple registry based RCTs) are available. Information on treatment effects in populations in clinical practice can be collected in pragmatic RCTs. Initiatives to decrease the administrative burden of RCTs are under way.

The TASTE trial is a registry based RCT that enrolled more than 7000 patients from clinical practice. Trial costs were approximately 10 times lower than those of a conventional RCT, and use of the inferior intervention decreased substantially after publication of the trial's results.[31] Instead of shifting clinical research to observational study designs, alternative, more robust methods for determining treatment effects in small populations should be developed further. Many approaches are currently under discussion (box 2). These efforts should be pursued in parallel to investigating the use of observational real world data in regulatory decision making.

The covid-19 pandemic has shown the importance of properly designed RCTs in a digitalised environment in routine practice. In particular, the Recovery trial has informed patient care with robust information at unprecedented speed.[41] Many of the lessons learnt in this success story can be transferred to trials in small populations. One important step would be to build a European trial infrastructure enabling the rapid set-up, conduct, and analysis of well designed, international, and registry based RCTs.

Combining such a scientific, technical, and administrative resource with a landscape of disease registries would enable robust data collection, also in smaller populations. DARWIN EU already integrates European disease registries. Limiting the scope of this major project to observational data is a missed opportunity. Instead, to increase its potential, DARWIN EU should be expanded to enable the conduct of registry based, pragmatic RCTs in routine practice settings.

The EMA is in the unique position of having an overview of new treatments under development. Thus, the agency would be able to identify opportunities for randomised multi-treatment adaptive platform trials, specifically in smaller populations. The number of these trials is also growing in late phase drug development, showing the feasibility of this concept.[34] The EMA and health technology assessment bodies could ensure that pre-registration platform trials not only meet the requirements of regulatory approval but also of health technology assessment. Giving regulatory bodies a mandate to initiate this type of study might support drug development in small populations more efficiently than turning to non-randomised study designs.

Healthcare and health policy decision makers require sufficiently robust evidence on the comparative effects of interventions. Involving them in defining a joint and comprehensive approach to evidence generation is the way forward to accelerate access to evidence based patient care.

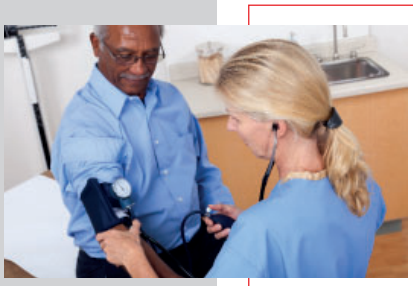
Beate Wieseler, head of drug assessment department beate.wieseler@iqwig.de
Thomas Kaiser, head of drug assessment department
Jürgen Windeler, director, Institute for Quality and Efficiency in Health Care, Cologne
Mattias Neyt, senior researcher
Frank Hulstaert, senior researcher, Belgian Health Care Knowledge Centre, Brussels

Cite this as: *BMJ* 2023;380:e073100

LETTERS Selected from rapid responses on bmj.com

LETTER OF THE WEEK

Stalled improvements in mortality predate the pandemic



The UK chief medical officers are right to be concerned about recent high mortality (Editorial, 11 February). They focus on the lower-than-expected uptake of important cardiovascular interventions and how increasing uptake might help. The framing of the causes of high mortality is, however, medicalised and individualised.

The stalled improvements in mortality, healthy life expectancy, and morbidity predate the pandemic, having been observed since around 2012 across the UK, with mortality worsening for those living in the poorest areas. The changed trends are seen in almost all causes of death (not restricted to cardiovascular disease) and almost all age groups. The leading cause of these stalled improvements is clearly economic—in particular the austerity policies implemented from 2010, which led to social security benefits being worth less in real terms (with more conditions put on their receipt) and to substantial cuts to public services.

Against this background, the pandemic had three effects. First, the direct additional mortality and morbidity caused by the virus. Second, substantial unmet healthcare needs as patients with covid-19 were prioritised by NHS services, and the public responded by reducing their own demands. Third, disruption to the social and economic lives of the population.

Austerity as an economic policy has not gone away, and we are left with a frayed social security system and public services that are now some way beyond underfunded and stretched. The past year has also seen rapid inflation of prices (without a commensurate increase in wages or benefit levels), leading to substantial reductions in real incomes. The effects of this on health are likely to be large and predominantly negative.

A closer look at the evidence of the effects of austerity and inflation, as well as the potential contribution from unmet healthcare need, is required to understand current UK mortality trends.

Gerry McCartney, professor of wellbeing economy; David Walsh, public health programme manager, Glasgow

Cite this as: *BMJ* 2023;380:p493

RESTORING AND EXTENDING SECONDARY PREVENTION

Treating tobacco dependence

The call to ensure a comprehensive approach to secondary prevention—defined by Whitty and colleagues as "evidence based, preventive measures to help stop or delay disease, taken during an interaction between an individual patient and a clinician"—is welcome (Editorial, 11 February).

I was surprised, though, to see no explicit mention of smoking. Across a wide range of long term conditions, smoking increases the risk of progressive deterioration in organ damage and of acute events. Treating tobacco dependence is arguably the single most effective secondary prevention approach available.

The Royal College of Physicians said in 2018 that the health benefits of quitting smoking accrue rapidly, and, unlike most interventions, investment in this area is associated with substantial in-year savings. It also noted the inadequacy of current responses to support the millions of adult smokers in the UK to quit. Tackling this will require focused attention; what goes unsaid will go undone.

Nicholas S Hopkinson, professor of respiratory medicine, London

Cite this as: *BMJ* 2023;380:p500

An interprofessional strategy is needed

Clinical intervention for the secondary prevention of cardiovascular diseases needs strengthening, as advocated by Whitty and colleagues. But how to do this with the shortage of healthcare providers and ageing populations? One path is the implementation of an interprofessional preventive strategy.

Providing comprehensive preventive services is a huge burden that is difficult for overwhelmed primary care physicians to fulfil. Growing evidence indicates that other healthcare providers should be involved, especially because the prevention of chronic diseases requires a complex mix of screening, lifestyle changes, and long term drug treatment. Interprofessional teams of nurses, pharmacists, and physicians might be optimal.

The multiplicity of actors around the patients allows flexibility in the provision of healthcare at a community level, eases continuity, and could reduce inequities in healthcare access. Implementing an interprofessional preventive strategy could also make secondary prevention easier to maintain during severe epidemics, helping mitigate the effects of disrupted healthcare services.

Arnaud Chiolero, professor of public health and epidemiologist, Fribourg
Valérie Santschi, professor of health services research, Lausanne

Cite this as: *BMJ* 2023;380:p505

INTRODUCTION OF INTEGRATED CARE SYSTEMS

NHS needs patient feedback, not mission statements

MPs have warned that the introduction of integrated care systems will not succeed unless government tackles longstanding problems in the NHS (This Week, 11 February).

Integrated care systems are a welcome, radical change to the ludicrous purchaser-provider system imposed on the NHS by Margaret Thatcher. They are most likely to help the NHS if they follow a government commitment to its original conception—a state provided health service, for all, free at the point of use. This means removing private providers from integrated care boards.

There will still be a deficit. The NHS has never been subject to direct democratic control. There would be scope for election through GP patient participation groups to a local body, which could advise every integrated care board. In a less directly democratic system, places could be reserved for councillors of the highest local authority. The NHS needs distilled patient feedback, not bureaucratic mission statements.

Richard L Symonds, retired consultant psychiatrist, Broadstairs

Cite this as: *BMJ* 2023;380:p476

DATA PRIVACY

Type 1 objections should not impede direct care

The case of a general practice [Summertown Health Centre in Oxford, right] withdrawing from an NHS commissioned pilot with a private company to provide kidney screening at home after three patients raised data privacy concerns is fascinating (News Exclusive, 28 January). Had type 1 objections been applied, other patients who had registered such objections could have justifiably complained that they were being inappropriately denied direct care.

Relying on implied consent to send data to a company to deliver direct care is problematic. An alternative approach would have been for practices to invite their patients to participate so that their consent was clear.

The roles of the various parties seem to be confused. The practice, not the integrated care board, would be the data controller and should carry out the data protection impact assessment. The pressures on primary care might leave little time for these assessments, but such pressures do not relieve data controllers of their responsibilities.

Paul Affleck, programme manager, Leeds

Cite this as: *BMJ* 2023;380:p518

A decade of confusion

The quick reaction to stop the pilot might not have been in the best interests of all patients in the practice.

Practices are busy and must be able to access clear and up-to-date guidance about correct and proportionate uses of patient data to aid their role as data controllers. There is an urgent need for this guidance, both for practices and their patients. The guidance must explain the ways in which patient data are used for direct care, including when this care provision is contracted by the NHS to a commercial partner. The guidance must also explain fully the different types of patient data opt-outs.

If we are all to benefit from lifesaving interventions, guidance about permissive uses of our data must be available to support practice teams. It is alarming that, a decade on from the introduction of type 1 opt-outs, there remains a clear lack of understanding of their purpose.

Alison Stone, coordinator; Chris Carrigan, expert data adviser, use MY data

Cite this as: *BMJ* 2023;380:p520

INDUSTRIAL ACTION

SAS doctors are also disenfranchised

Limb describes the growing dissatisfaction of NHS consultants, junior doctors, and GPs (News Analysis, 11 February). But he has not included arguably the most disenfranchised part of the medical workforce: SAS doctors (specialty doctors, associate specialists, and specialists) and locally employed doctors. The General Medical Council says that, should trends continue, SAS and locally employed doctors together will become the largest register group in the medical workforce by 2030. It is therefore disappointing to see them excluded from this discussion.

SAS doctors have a similar age profile to the consultant workforce. Many are similarly taking early retirement, disheartened by pay erosion or simply succumbing to burnout in an overstretched NHS. Many trusts rely heavily on these doctors to provide direct patient services. SAS doctors were recently consulted by the BMA on pay and their attitudes to potential industrial action. Any such action would be highly disruptive, and all of this is worth reporting. Our exclusion continues to undermine us.

Imran Sharieff, specialty doctor in anaesthesia, London

Cite this as: *BMJ* 2023;380:p508

Ask the government questions and wait for the answers

It is crucial to ask the government specific questions and to wait for the answers; silence is a powerful bargaining tool. When will the workforce plan be published, for example?

Which other public safety professions would the government allow to function while 13% understaffed? If an HGV driver is required by law to stop driving after a set number of hours for safety reasons, why is it acceptable for doctors or nurses—those directly responsible for human lives—to work almost double their hours, with no breaks?

The government wants a high skills and high wage economy. Doctors are among the most highly skilled professions. Are doctors not included in the government's intentions?

Why does the government blame the "independent" pay review bodies for minimal pay recommendations, when the government sets the financial parameters for such recommendations? Will the government ask these bodies to make appropriate recommendations without constraint?

Hannah Walker, retired RAF officer, Thornford

Cite this as: *BMJ* 2023;380:p512

TACKLING RACE INEQUALITY IN THE MEDICAL WORKFORCE

Recognising attainment rather than failure

I welcome the NHS England Workforce Race Equality Standard team's plan to improve diversity and equality in the NHS, particularly increasing diversity in senior leadership (Editorial, 11 February). Having more leaders who can relate to being an international medical graduate or a doctor from an ethnic minority is key. I agree, however, that the plan lacks explanation of any accountability for failure in implementing these actions.

Rather than a penalty for failure, a system where attaining diversity and equality is recognised might be more enticing. The Athena Swan scheme recognises universities and research institutions striving for gender equality and advancement of women in academia and leadership. Attaining Athena Swan bronze, silver, and gold awards is seen as desirable and creates better awareness.

No system is perfect, but being open to new, unconventional ways to make sustainable changes in a giant organisation like the NHS would be the first step.

Wahyu Wulaningsih, clinical oncology specialty trainee year 3, London

Cite this as: *BMJ* 2023;380:p490

OBITUARIES

Richard Martin Oliver

Consultant interventional cardiologist Hull University Teaching Hospitals NHS Trust (b 1958; q London, 1980; MD (Soton), FRCP, FESC), d 13 February 2022

Richard Martin Oliver was appointed as a consultant interventional cardiologist at the Ipswich Hospital NHS Trust in Suffolk in 1993, where his arrival had an immediate impact on cardiological services across east Suffolk and north Essex. He was instrumental in delivering invasive therapeutic and imaging techniques, and in establishing the rapid assessment cardiac chest pain clinic and thrombolysis pathway after acute myocardial infarction. In 2003 he was appointed at the Hull University Teaching Hospitals NHS Trust. Richard remained active in research throughout his career, publishing scientific papers and book chapters, and acting as principal investigator for an array of multicentre research studies. Outside work Richard enjoyed gardening and watching sport, particularly golf and Formula 1 motor racing.

William M Oliver

Cite this as: *BMJ* 2023;380:p359

Allan Philip Radford

GP (b 1920; q Bristol, 1944), died from old age on 26 December 2022

After hospital posts in medicine, fevers, and pulmonary tuberculosis, Alan Philip Radford ("Philip") was called up, serving in Egypt, Palestine, and Greece. On entering general practice, he worked as an assistant in Gloucestershire, in the days when the doctor dispensed medicines and carried out home midwifery. In 1951 he moved to Bristol as a GP, working first in partnership (also as a part time prison medical officer and member of the local medical committee). In 1964 he became a singlehanded GP. Philip retired in 1980 to a thatched cottage on the Quantock Hills in Somerset. He and his wife, Rosemary, developed a colourful and productive garden and Philip was able to follow his lifelong hobby of natural history, writing articles on birds and insects. He leaves two daughters, grandchildren, and great grandchildren.

Ursula Salzman

Cite this as: *BMJ* 2023;380:p358

Mary Mabel Tannahill

Consultant psychiatrist Clwyd Health Authority (b 1932; q Glasgow, 1957; DPH, DPM, FRCPsych), died from dementia of old age 7 December 2022

Mary Mabel Tannahill ("Mabel") was the only child of Andrew Robert Tannahill (poet, writer in Scots, and translator) and Mary Reid (artist), members of the cultural elite of Glasgow. Mabel trained in public health before switching to psychiatry. She was a part time senior lecturer and honorary consultant at St Thomas' Hospital, London, before her husband's job as a company doctor for Unilever took him to Liverpool. Mabel was appointed consultant at the North Wales Hospital in Denbigh. She was with Clwyd Health Authority from 1975 to 1994. After the premature death of her first husband she met and married David Jones, the chief administrative medical officer for Clwyd. Mabel leaves David, two sons from her first marriage, two granddaughters, and a grandson.

Peter McGuffin

Cite this as: *BMJ* 2023;380:p368

Jenny Eastwood

Consultant psychiatrist (b 1935; q Edinburgh, 1960; DPM, FRCPsych), died from metastatic carcinoma of the transverse colon on 11 November 2022

Jenny Lucas met Martin Eastwood—from Yorkshire, like Jenny herself—in her first week at medical school. They married in 1958 and she combined early motherhood with part time employment in public health and general practice. In the 1970s she started training in psychiatry and in 1983 was appointed consultant psychiatrist to Fife Health Board. Her enthusiasm, clear thinking, and calmness allowed her, with consultant colleagues, to reconfigure mental health services in Fife. Jenny and Martin (a consultant gastroenterologist) published journal articles on the psychiatric aspects of irritable bowel syndrome. After retiring in 1995, they returned to Beverley. Jenny leaves Martin, four children, and nine grandchildren.

Martin Eastwood, Bill Dickson

Cite this as: *BMJ* 2023;380:p363

Iain Huddleston

GP (b 1933; q St Andrews, 1957), died suddenly from cardiovascular disease on 13 December 2022

Iain Huddleston's first job was at Staincliffe Hospital, where he met another junior doctor, his future wife, Sheila Russell Crosland. On returning from national service in Ghana, he completed a six month obstetrics post in Chester, followed by one year as a trainee GP in Peebles. He moved to Blairgowrie in May 1962 and hatched the idea for superb, patient friendly, modern premises and realised that vision by driving forward the conversion of a disused mission hall. Iain retired in October 1993 and subsequently underwent successful coronary artery surgery. This bought him many more years than expected but eventually his vascular disease progressed. Iain leaves Sheila, three children, five grandchildren, and five great grandchildren.

Alasdair Shaw

Cite this as: *BMJ* 2023;380:p361

Alan William Frederick Lettin

Orthopaedic surgeon (b 1931; q University College Hospital, London, 1956; FRCS Eng, MS), died from old age on 3 January 2023

Alan William Frederick Lettin entered orthopaedic training mainly at the Royal National Orthopaedic Hospital. In 1967 he was appointed as a consultant orthopaedic surgeon to Barts and Queen Elizabeth Hospital, Hackney, and in 1969 he was appointed to the Royal National Orthopaedic Hospital while relinquishing his appointment at Queen Elizabeth Hospital. He was involved with the development of the Stanmore knee, elbow, and shoulder replacements and demonstrated them around the world. His name was in over 40 peer reviewed publications, 37 chapters in books, and several books. In retirement Alan moved to Suffolk. His wife, Pat, predeceased him in 2018. He leaves three of their four children.

Keith Tucker, John Getty, Jonathan Lettin

Cite this as: *BMJ* 2023;380:p360

Nael Shihabi

UK trained cardiothoracic surgeon who founded Palestine's first medical school

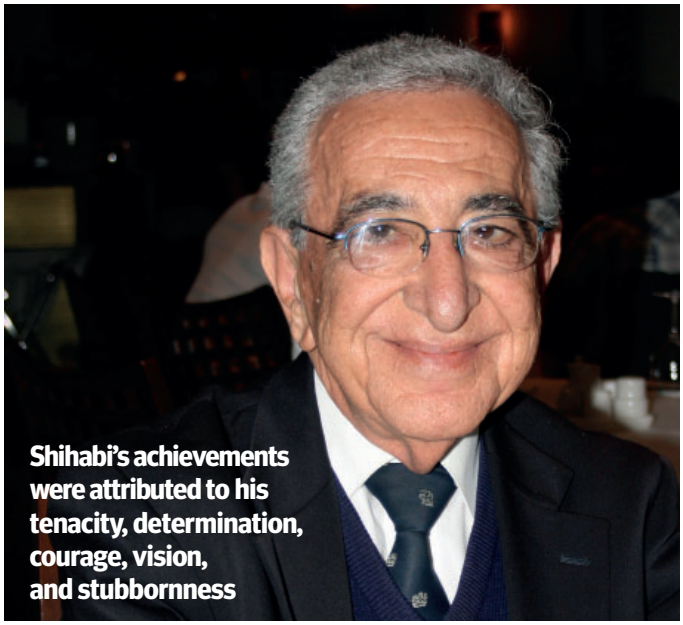
Khalil Nael Shibai (b 1936; q Alexandria, Egypt, 1959; LMSSA, FRCSE), died from pneumonia with septic shock and kidney failure on 21 November 2022

After 10 years in the UK, Nael Shihabi was looking forward to what should have been a glittering career as a consultant cardiothoracic surgeon. He was passionately committed to the NHS, which he saw as a triumph for the socialist ideal that treatment should be free at the point of use. But when his father died in 1973, making him the new head of his family, he felt duty bound to return home to Amman.

Leaving the NHS was the biggest regret of his life, but his sacrifice became Palestine's immense gain. After helping to develop Jordan's first medical school in Amman (established in 1971), he founded the first Palestinian medical school in Jerusalem in 1994. He was also one of the driving forces behind the formation of the Palestinian General Medical Council in 1998.

Shihabi's achievements were attributed to his tenacity, determination, courage, vision, and stubbornness. His complaints that medical services in the West Bank were "not up to an acceptable standard" were vehemently dismissed. Most Palestinian doctors had been trained in Soviet Bloc countries—including Bulgaria, Hungary, and Romania—at little or no expense. An American doctor who wanted to develop a private hospital in Palestine and bring money into the country also opposed Shihabi—further hardening opposition against him.

The first intifada uprising in the conflict between Israel and Palestine (1987-93) also hindered Shihabi's plans and took him to the medical front line at the Makassed Hospital, Jerusalem. Writing in the *Jordan Medical Bulletin*, he described one shift running from 10.00 am to 1.00 am the following day: "The first two wounded patients arrived 15 minutes apart. While dealing with the first one who had a shattered left lung from a high velocity bullet, the second patient arrived, almost dead."



Shihabi's achievements were attributed to his tenacity, determination, courage, vision, and stubbornness

He clamped the hilum of the lung of the first patient to stop the bleeding temporarily and covered the wound. Turning to the second patient he repaired his shattered, bleeding lung before returning to the first patient. Both survived.

Israeli press reports about an Arab surgeon operating simultaneously on two patients surprised the hospital administrators, who later asked Shihabi if they were true.

Shihabi's formidable surgical reputation won him an audience with the Palestinian president Yasser Arafat—resulting in a presidential decree that Palestine should have its own medical school. Opposition immediately melted away.

The Islamic Bank in Jeddah donated the cost of a building. Japanese donors provided all laboratory equipment. Kuwait contributed to the library. The school, in Al-Quds University, opened in October 1994 with 32 students. Shihabi's experience in developing Jordan's first medical school made him first choice as founding dean. He also took the chair in cardiothoracic surgery.

Early life and career

Shihabi was born in Jerusalem. After attending Hashemite School in Ramallah, where his father was headmaster, he moved to Alexandria amid concern about political stability after the 1948 Arab Israeli war. Finishing top of his class, he read medicine at Alexandria University.

After working in Kuwait and volunteering in Algeria with the Kuwaiti Medical Mission, Shihabi completed training jobs in the UK and co-founded Palestinian Medical Aid, a charity established in 1967 during the six day war. (The charity, later re-named Medical Aid for Palestinians, is still active.)

When he returned home to Amman, a doctor friend suggested that he should contact Fuad Kilani, minister of health for Jordan, who offered him a job in the Amman Civic Hospital, which was under construction and to become affiliated to Jordan University.

Contacts in high places are not always a blessing. The hospital refused to open a cardiothoracic department, arguing that there was already a unit in the Royal Medical Service. Shihabi also had to use his own surgical instruments and endoscopes for two years before the hospital obtained its own supplies.

He found consolation for seven years in a love of teaching and other duties which, in effect, became his apprenticeship for the far bigger role he was to assume in establishing Palestine's first medical school. He became secretary of the faculty council, a member of the university council and a co-founder of the scientific and cultural committee. He also published a quarterly journal, *Horizon*, which reflected his passion for drawing and photography. He drew all his medical illustrations for slides for his talks and lectures.

But seeing no further prospects at the university, he resigned and set up in private practice in Amman, only to find that this did not align with his values—the values he associated with the NHS. Shihabi moved to the Makassed Hospital, Jerusalem, where he set up a cardiothoracic department. Remarkably, he continued operating until his early 80s, when he broke his hip in an accident.

He married Fatina Qutob in his early 50s. She survives him.

John Illman, London
john@jicmedia.org

Cite this as: *BMJ* 2023;380:p76