EDITORIALS

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UK law on consent finally embraces the prudent patient standard

But it will take much more to change clinical practice

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The UK Supreme Court's decision in the Montgomery case is a landmark judgment, establishing beyond doubt the court's commitment to protecting patients' right to self determination.[1] The judgment concerns Nadine Montgomery, a woman with diabetes whose son was born with serious and permanent disabilities after a shoulder dystocia during delivery (pictured, right). Montgomery's obstetrician had not warned her of the risk of shoulder dystocia during vaginal delivery or discussed alternatives such as caesarean section.

The court held that the doctor should have done both: doctors have a duty to ensure that each patient is aware of any material risks of any recommended treatment and of any reasonable alternative treatments. The test of materiality is whether a reasonable person in that particular patient's position would be likely to attach importance to the risk, or whether the doctor is—or should reasonably be—aware that that particular patient would be likely to attach importance to it. The message for clinicians is: know your patient and provide tailored information.

> The emphasis is not on the patient's understanding of information but on his or her signal that the doctor may proceed with treatment

The patient must be given sufficient information, but what constitutes sufficient? Two standards of disclosure have been employed: the professional standard (the court relies on medical opinion) and the "prudent patient" standard (the court considers what a reasonable person would want to know to make an informed choice).

The requirement for full disclosure of material risks to the patient, with the standard of disclosure being determined not by the medical profession but by the court, is known as the legal doctrine of informed consent. This doctrine is well established in many US jurisdictions, Canada, and Australia, but the courts resisted its incursion into the UK for decades. The definitive UK position (before the Montgomery case) on this doctrine was established by the House of Lords in the case of Sidaway.[2] The court ruled that the doctrine of informed consent did not apply in the UK and endorsed the

Patients have a right to self determination

position articulated in the case of Bolam that: "a doctor is not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men."[3]

The courts do, however, move with the times, and there has been a gradual but steady shift away from the professional standard. The case of Bolitho established that if professional opinion does not withstand logical analysis the judge is entitled to hold that the body of opinion is not reasonable or responsible.[4] In the case of Pearce the Court of Appeal stated that "a doctor's decision not to disclose risks will now have to be subjected to logical analysis," and if he has withheld information without good reason "he will be liable even though his decision may have been consonant with ordinary professional practice."[5]

More recently, in the Chester case the House of Lords side stepped the traditional requirement to prove causation (that is, had the claimant been warned of the undisclosed risk, she would not have had the treatment) in order to protect the patient's right to self determination.[6] And in the case of Birch, the High Court stated that the duty to disclose significant risks included information about alternative treatments.[7] The Montgomery case thus marks the final stage of the UK courts' transition from the professional standard to the prudent patient standard.

Potential effect (or lack of it) on clinical practice

While this is a landmark judgment, its effect on clinical practice could be limited unless a concerted effort is made to reconceptualise consent on the shop floor. Current professional guidance on consent already approximates to the prudent patient standard, advising doctors to provide information that the patient would want to be given.[8-11] The position of the Supreme Court on the importance of dialogue in consent transactions, the need to ensure that the patient understands the information provided, and the therapeutic privilege (whereby a doctor may withhold information from a patient if disclosing it would cause serious psychological harm) is consonant with published professional guidance.

However, the model of consent that is applied in actual practice (contrived consent) differs from that described in professional guidance (bona fide consent). Bona fide consent is where the patient makes an informed choice after a dialogue with the doctor, in a collaborative relationship. In contrived consent, the patient is presented with a menu of choices and a response is elicited. The menu may be accompanied by a large quantity of information, most of it not specific to the patient, or little or no information. The emphasis is not on the patient's understanding of information but on his or her signal that the doctor may proceed with treatment. In most consultations the signal is verbal, but for surgery it is usually a signature.

The current model relies heavily on consent forms. But many clinicians are unaware that consent can be valid without a signed consent form (it is the patient's informed choice that constitutes consent, not the form), while consent can be invalid even though a consent form has been signed (because the patient has not made a self determining, informed choice).

Contrived consent has prevailed despite the abundance of legal, ethical, and professional guidance on bona fide consent, because of deficiencies in doctors' and patients' perceptions of consent. Health professionals do not know enough about the law of consent, and patients see the consent process not as a means to protect their rights but as a means of protecting the doctor from litigation.[12 13] Medical professionalism demands that the gap between the ideal and the operationalised methods of consent should be closed. Medical schools, royal postgraduate medical colleges, and service quality regulators must take up this difficult challenge.

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- Endgames: Meta-analysis: testing for reporting bias (*BMJ* 2015;350:g7857)
- Editorial: Reporting of harms in systematic reviews and their primary studies (*BMJ* 2014;349:g6819)
- Research: Selective reporting bias of harm outcomes within studies (*BMJ* 2014;349:g6501)

Selective trial reporting: betraying trial participants, harming patients

Reporting biases found in trials of cardiovascular devices

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Worrying differences between trial information submitted to the FDA and what's reported in medical journals

Reporting biases in published trials were first identified in 1986.[1] Published randomised studies of combination chemotherapy compared with an alkylating agent as treatment for ovarian cancer showed a significant survival advantage for combination chemotherapy. Unpublished cancer trial registry data from the same studies, however, showed no such advantage.[2] Similarly, in the treatment of multiple myeloma, registry data suggested a smaller survival advantage for combination chemotherapy than the results of published studies.

The author who reported the discrepancy concluded that his findings "demonstrate the value and importance of an international registry of all clinical trials."[1] Subsequent evidence for biased and selective reporting included prompt or delayed publication depending on whether trial results were positive or negative[3] and more favourable results and conclusions in published studies funded by industry than in those funded independently.[4]

The linked paper by Chang and colleagues shows similar reporting biases in trials of medical devices.[5] The authors found worrying differences between trial information submitted to the US regulator (the Food and Drug Administration) and trial information reported in medical journals. Among 177 studies of 106 high risk cardiovascular devices submitted to the FDA, fewer than half were published, and fewer than half the published studies (45%) reported primary results that precisely matched the results in submissions to the regulator. Among the published primary results, 11% (17) were judged to be "substantially different" from those submitted to the FDA. The authors concluded that "even when trials are published, the study population, primary endpoints, and results can differ substantially from data submitted to the FDA."[5]

Most studies of reporting biases have examined differences in efficacy between unpublished clinical trial data and journal publication data but evidence now exists of under-reporting of adverse events. A recent *BMJ* editorial cites "the growing body of research on reporting biases, which documents the gross under-reporting of adverse event data in such [medical journal] sources."[6]

> Two pharmaceutical companies sued the European Medicines Agency and the agency has watered down its original plans

Unfortunately, selective reporting of clinical trial data in journals also extends to companies' selective non-reporting of safety data. In 2012, the US Department of Justice announced that "GSK [GlaxoSmithKline] has agreed to plead guilty to failing to report data to the FDA and has agreed to pay a criminal fine in the amount of $242,612,800 for its unlawful conduct concerning Avandia . . . The United States alleges that, between 2001 and 2007, GSK failed to include certain safety data about Avandia, a diabetes drug, in reports to the FDA that are meant to allow the FDA to determine if a drug continues to be safe for its approved indications and to spot drug safety trends."[7]

Industry backlash

Efforts to increase the public availability of clinical trial data to prevent the serious public health consequences of overstating benefits and understating risks have triggered strong industry opposition. In 2012 the former executive director of the European Medicines Agency (EMA), Guido Rasi, committed the regulator to "proactive publication of clinical-trial data, once the marketing-authorisation process has ended." He added "We are not here to decide if we publish clinical-trial data, but how."[8] Two pharmaceutical companies sued the EMA to prevent disclosure, and the EMA has watered down its original plans.[9]

Beyond adverse effects on patients of selective reporting in medical journals, the absence of publicly available data from clinical trials violates an important ethical principle of the Declaration of Helsinki: "Researchers have a duty to make publicly available the results of their research . . . Negative and inconclusive as well as positive results must be published or otherwise made publicly available."[10] Many people participate in research because they trust that the published results might improve the health of the general population.

Ignoring the Declaration of Helsinki, in 2013 the Pharmaceutical Research and Manufacturers of America (PhRMA) urged the US government to influence the European Union against the EMA's data disclosure policy. In a letter to a US trade representative, PhRMA wrote that "Disclosure of companies' non-public data submitted in clinical and pre-clinical dossiers and patient-level data risks damaging public health and patient welfare."[11]

It is clear that the reverse is true. Non-disclosure is far more damaging. The letter of rebuttal from leaders of the high profile campaign for public registration and reporting of all trial results (AllTrials) reads, "The world is moving towards a recognition that hiding information about what was done and what was found in clinical trials is an abuse of trial participants' trust and exposes patients to unnecessary harm."[12]

I, and many others, agree.

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RESEARCH, p 12

Urinary incontinence in women (*BMJ* 2014;349:g4531)
Research: Effect of pelvic floor muscle training compared with watchful waiting in older women with symptomatic mild pelvic organ prolapse (*BMJ* 2014;349:g7378)
Research News: Poor long term outcomes after prolapse surgery (*BMJ* 2013;346:f3091)

Mesh use in surgery for pelvic organ prolapse

Despite many advances, outcomes after surgery remain far from perfect

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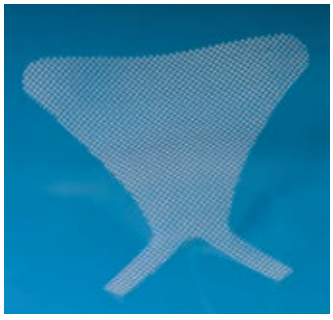
By age 80 years, one in eight women will undergo surgery for pelvic organ prolapse (POP), a condition where the pelvic organs descend into or through the vaginal canal.[1] In the United States, about 80% of procedures are performed transvaginally.[2-4] Building on the experience of general surgeons and the treatment of abdominal hernias, pelvic surgeons began using synthetic mesh to augment prolapse repairs to reduce prolapse recurrence seen frequently after native tissue (non-mesh) repairs. However, use of synthetic mesh also results in increased adverse events, in some cases with serious consequences.[2 5] As a result, the use of mesh for transvaginal POP surgery has been the source of much scrutiny, including two public health notifications from the US Food and Drug Administration (FDA), a change in the US regulatory process for mesh devices, and substantial litigation.[2 6]

In a linked article, Chughtai and colleagues report on mesh use and risk of complications and reintervention of POP surgeries from a large, population based cohort from New York state between 2008 and 2011. Overall, 26% of the 27 991 patients in the cohort received mesh as part of their POP surgery. In a propensity matched analysis, mesh recipients had a 66% higher rate of undergoing at least one reintervention (3.3% *v* 2.2%) within a year after surgery, compared with non-mesh recipients. Mesh recipients also had a higher risk of urinary retention. This study provides important real world data to complement existing clinical trial data evaluating the safety and efficacy of mesh use for POP repair.

A meta-analysis of clinical trials indicated that transvaginal mesh augmentation for anterior vaginal prolapse resulted in better anatomical and symptomatic outcomes one year after surgery than those from non-mesh repairs.[5] However, mesh use is associated with an 11.4% rate of mesh erosion, 6.8% rate of reoperation for complications, increased prolapse recurrence in the posterior and apical segments of the vagina, and increased stress urinary incontinence after surgery.[5]

The population level data provided by Chughtai and colleagues show a much lower reintervention rate in the year after POP mesh surgery (3.3%) than that seen in clinical trials, and smaller differences in complications between mesh and non-mesh repairs. Therefore, this real world application of transvaginal mesh may be associated with less risk than suggested by clinical trials. However, the linked study provides no data on relative effectiveness beyond reintervention, and is unable to differentiate between reinterventions for recurrence and reintervention for complications.

Chughtai and colleagues also provide novel information about mesh use over the four year period between the two FDA public health notifications. In 2008, the FDA issued its first notification informing clinicians and patients about adverse events associated with mesh use for pelvic reconstructive surgery, noting that "although rare, these complications can have serious consequences."[2] Despite the FDA notification, mesh use for POP surgery in New York state increased from 21% in 2008 to 30% in 2011. However, data from the cohort were not available beyond 2011 when the FDA issued their second and more consequential notification indicating that, based on increased adverse event reporting and their review of the literature, "serious complications associated with surgical mesh for transvaginal repair of pelvic organ prolapse are *not rare*."[2] The notification concluded that it is unclear whether transvaginal POP repair with mesh is more effective than traditional non-mesh repair in all patients with POP, and that it may expose patients to greater risk.[2]



More redos

Litigation

The consequences were substantial. In January 2012, the FDA issued orders requiring mesh device manufacturers to perform post-market surveillance studies. They also indicated their intent to change the regulatory pathway for transvaginal mesh products so that pre-market approval studies demonstrating safety and efficacy would be required before approval and marketing; a requirement not mandated previously for most mesh devices. The notification prompted a whirlwind of litigation, resulting in over 70 000 legal claims against nine device manufacturers, and many device companies chose to exit the market in the US and worldwide.[6]

Medical professional societies issued guidance about appropriate indications for POP mesh use, surgeon credentialing, informed consent, and risk mitigation.[7-9] In a joint committee opinion, the American College of Obstetrics and Gynecology and American Urogynecologic Society concluded that POP vaginal mesh repair should be reserved for high risk individuals in whom the benefit of mesh placement may justify the risk, such as those with recurrent prolapse or medical comorbidities that preclude more invasive open and endoscopic procedures; a sentiment echoed by many other medical societies internationally.[8 9]

Recent data from the Organization for Economic Cooperation and Development (OECD) countries showed an overall decrease in transvaginal mesh use in 2010-12.[10] However, there was substantial variation between countries—for instance, a 47% decrease in the USA and a few countries showing an increase in use. The United Kingdom had the lowest rate of mesh use (3.4%) in this study.[10] The decrease in transvaginal POP mesh use has been accompanied by an increase in the use of abdominally or laparoscopically placed mesh for POP repair (sacrocolpopexy).[5] Current data suggest that sacrocolpopexy has better efficacy for non-mesh repairs of prolapse of the vaginal apex and lower rates of complications than mesh placed vaginally; however, the long term rate of mesh exposure could still be as high as 10.5%, five to seven years after surgery.[11]

POP can have a substantial effect on a woman's quality of life.[12] Despite many advances, outcomes after surgery remain far from perfect. Decisions about surgical approach, including whether to use mesh, require a careful balance of risks and benefits. Policy makers and regulatory agencies must continue to promote policies that protect patient safety while encouraging innovation and shared decision making. Research that better characterizes the factors associated with risks and benefits of mesh use are sorely needed to assist this shared decision making process.

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RESEARCH, p 13

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- News: Former editor pays $1m to settle allegations of kickbacks to promote products (*BMJ* 2015;350:h1459)
- Editorial: Medical journals and industry ties (*BMJ* 2014;349:g7197)
- Head To Head: Has the hunt for conflicts of interest gone too far? (*BMJ* 2008;336:476)

Revisiting the commercial-academic interface in medical journals

The *New England Journal of Medicine* goes on an ill advised journey

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Public trust in the pharmaceutical and biotechnology industry is low.[1] Many practising physicians share that mistrust and are inclined to discount the results of otherwise sound studies that are industry funded.[2 3] There are good historical reasons to be sceptical. But has suspicion degenerated, as some have charged, into "mindless demonisation?"[4] The *New England Journal of Medicine* (*NEJM*) seems to think so. It has published a series of commentaries and an editorial suggesting there have been serious negative consequences of strict, "oversimplified" conflict of interest and disclosure policies, including the development of a "hostile climate" and "loss of trust."[5-8] Editor in chief, Jeffrey Drazen, says the "divide" between academic researchers and industry is not in the best interests of the public because "true improvement can come only through collaboration."

A close reading of Drazen's editorial suggests he is having second thoughts about policies put in place by many journals—including *The BMJ*—that make it "harder and harder for people who have received industry payments or items of financial value to write editorials or review articles . . . Having received industry money, the argument goes, even an acknowledged world expert can no longer provide untainted advice."[9] These policies, he says, came about "largely because of a few widely publicized episodes of unacceptable behavior." He urges revisiting of the reasons that "medical journal editors remain concerned about authors with pharma and biotech associations."

We are deeply troubled by a possible retreat from policies that prevent experts with relevant commercial ties from writing commentary or review articles. The pharmaceutical and biotechnology industries may well be our medical saviours, but that is not a good reason to return to past practices. Such policies were not motivated solely by a few events, as Drazen asserts, but by recognition of extensive, systemic problems. These problems are far from solved, including internationally, as shown by recent events in India and China.[10 11]

Checks and balances remain important

We agree that people with industry affiliations may be capable of expressing impartial views about matters affecting the commercial interests with which they are associated. Journal readers and editors, however, have no reliable way of identifying which industry affiliated views are disinterested and which are inappropriately influenced by commercial considerations, particularly in subtle ways. Bias is not always overt or easily detected. Authors with industry ties may be likely to approach a topic from a perspective shaped by their associations, so that their views will reflect industry assumptions, priorities, and preferences. The existence of academic and non-financial conflicts of interest does not reduce the need to be wary about conflicts that arise out of the powerful economic incentives associated with industry connections.

> Some academics must work closely with industry to develop and commercialise new medical treatments, but they should not also write editorials, reviews, or guidelines that appraise them

In our view, no one has such superior knowledge that he or she is the only one qualified to write an article on a subject. Checks and balances are important in any system. In the case of medical evidence, they should be based on the assumption that it is a mistake to combine evidence production and appraisal functions in a single person or group. Some academics must work closely with industry to develop and commercialise new medical treatments, but they should not also write editorials, reviews, or guidelines that appraise them. These are different professional responsibilities, and they clash.

The stakes are high. Editorials, reviews, and guidelines legitimise medical knowledge and shape clinical practice. Society needs a group of people who can evaluate medical evidence completely free of the appearance of commercial taint. One goal of *The BMJ*'s zero tolerance policy on education pieces by authors with industry ties was to offer unconflicted authors "prominence and visibility." The success or failure of this policy can be evaluated only after the distinction between these different responsibilities—developing treatments or evaluating their place in practice—has been established long enough to influence the career choices of young doctors.

Revisiting the Commercial–Academic Interface

Jeffrey M. Drazen, M.D.

In the mid-1940s, Selman Waksman, a soil microbiologist, and his team discovered streptomycin, an antibiotic with action against the tubercle bacillus.[1] Although he was able to show efficacy in the laboratory, Waksman realized that if his discovery was to be of value to the world, he needed a partner capable of manufacturing adequate amounts of the material under conditions that would make it suitable for use in humans. He therefore struck a deal with Merck to produce streptomycin for clinical use.[2] Soon thereafter, the British Medical Association undertook a large randomized, controlled trial of streptomycin for the treatment of tuberculosis. The results, including a description of the utility of streptomycin and resistance to it, were published in the *British Medical Journal*.[3] This partnership between an academic researcher and a drug company went on to alleviate substantial human suffering and should be a model for current behavior. Unfortunately, it is not.

In 1950, Waksman, who was arguably the world's leading authority on antibiotic treatment of tuberculosis and who 2 years later received the Nobel Prize in Physiology or Medicine, was the sole author of a review article on streptomycin and neomycin published in the *British Medical Journal*.[4] That would most likely not happen today. Over the past two decades, largely because of a few widely publicized episodes of unacceptable behavior by the pharmaceutical and biotechnology industry, many medical journal editors (including me) have made it harder and harder for people who have received industry payments or items of financial value to write editorials or review articles.[5] The concern has been that such people have been bought by the drug companies. Having received industry money, the argument goes, even an acknowledged world expert can no longer provide untainted advice.

But is this divide between academic researchers and industry in our best interest? I think not — and I am not alone. The National Center for Advancing Translational Sciences of the National

Second thoughts

Disclosure does not solve the problem of bias and might make it worse. Advisers who disclose conflicts may subsequently feel more comfortable giving biased advice, a phenomenon called moral licence. Those who receive advice from a biased adviser often do not discount it sufficiently.[12] Finally, "requiring disclosure is much easier than changing the status quo . . . I'd rather tell you I'm on the gravy train than get off it."[13]

We don't find much to agree with in *NEJM*'s anecdotal analysis, but we do agree that criticism of the pharmaceutical and biotechnology industry is often reflexive and unfair. In fact, industry leads academia in complying with trial registration and reporting requirements.[14] Many companies have embraced the open data movement.[15] These are good things, but improvements in obvious problems should not be a pretext for regressive change.

Instead, we should encourage all medical journals to separate the functions of evidence generation from those of appraisal. Policies that prevent experts with commercial ties from participating in evidence evaluation institutionalise this protection instead of making it optional. They are an important safeguard against bias and a defence against the perception of a "trial-journal pipeline" in which "companies treat trials and journals as marketing vehicles."[16] We agree with Steinbrook and colleagues that journal editors have a responsibility to lead on this issue and that "financial conflicts of interest in medicine are not beneficial."[17] It is a mistake by *NEJM* to suggest that rigorous standards should be revisited. To do so would undermine the trustworthiness of medical journals and be a disservice to clinical practice and patient safety.

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PERSONAL VIEW, p 24