LETTERS

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BMJ OPEN DATA CAMPAIGN

Time to move the debate forward

Few arguments can be made for withholding clinical trial data.[1] One is an ethical issue over patient confidentiality; another is that disclosure leads to patient harm.

The drug industry understands the potential influence of academics, and rewards can be substantial. For example, according to Roche's 2011 financial report, John Bell received 390 000 Swiss Francs (£260 450; €322 450; $420 000) last year for his role on the board of directors.[2] What do Roche and its shareholders expect for this level of involvement and remuneration? And, how could this role facilitate the scientific scrutiny that the Cochrane group is trying to apply to trial data for oseltamivir, by helping to ensure that Roche honours its commitments to allow access to these data?

The proponents of trial non-disclosure often quote the potential harms, yet reports of such harms are hard to find. By contrast, open disclosure has substantial benefits. For example, in the Antithrombotic Trialists' Collaboration, 287 different studies contributed patient level data to the effects of antiplatelet drugs for patients at high risk of occlusive vascular events.[3] Moreover, vast databases such as the Clinical Practice Research Database and the National Joint Registry routinely use patient level data to inform practice: why is it therefore so difficult to obtain clinical trial data?

The substantial "speaker fees" that many clinicians and clinical academics receive (more than $100 000 in some cases) have prompted some public universities in the US to propose banning such activities, given the potential for conflicts of interest and their influence on policy and practice.[4] Many of these conflicts have come to light only since new rules in the US now encourage drug companies to publicly disclose all fees paid to academics.[5] These measures are important, given that financial relationships can influence the results of scientific studies.[6]

The European Medicines Agency and the *BMJ* are making great strides in improving access to clinical study data, to ensure that practice is based on transparent evidence. Yet, many manufacturers and clinical academics are uneasy with proactive disclosure of data and financial relationships. At a time when the drug industry wants stronger ties with academia, there is a need for greater scrutiny.

We suspect many colleagues in clinical academia share our views, and we look forward to moving the debate forward so that we can develop a more transparent and conflict-free policy towards accessing data.

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1 Godlee F. Open letter to Roche about oseltamivir trial data. *BMJ* 2012;345:e7305. (29 October.)
2 Roche Finance. Finance report 2011:162. www.roche.com/investors/annual_reports/annual_reports_2011.htm.
3 Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. Antithrombotic Trialists' Collaboration. *BMJ* 2002;324:71.
4 Budnick N. Oregon Health and Science University may ban faculty from pharmaceutical industry speakers' bureaus. www.oregonlive.com/health/index.ssf/2012/11/oregon_health_science_universi_14.html.
5 Burstein HJ. Disclosing pharma payments to oncologists: what will we learn? *J Natl Compr Canc Netw* 2012;10:133-4.
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DATA SHARING AMONG TRIALISTS

Let's share all study materials

Rathi and colleagues provide insight into clinical trialists' opinions and experiences of sharing clinical trial data.[1] We would like to raise two related matters.

Firstly, this study and previous studies cited within are limited to sharing data. We suggest that questionnaires, intervention manuals, analysis scripts (such as syntax files), output files, and other materials that are used to generate study reports should also be shared. Accurate replication requires these additional materials. This is essential for scientific progress because successful replication strengthens our evidence that a given theory, model, or assumption holds, whereas unsuccessful replication is our only means of disproving them.[2] Publication of analysis scripts and output files is necessary because researchers make many important choices that are not disclosed in research articles.[3]

Secondly, the concerns about data sharing raised by Rathi and colleagues' respondents can mostly be refuted.[4] For example, one concern was the ability to publish own research. When a researcher wants to publish several articles about one dataset, publishing the dataset before all articles are published can be risky, because others might conduct analyses that had been planned for later articles and publish them earlier. A solution is not to publish the entire dataset but only those variables described in published articles. This is related to another identified reason: sufficient academic or scientific recognition. In the rat race of "publish or perish," it might seem that publishing materials (such as data, questionnaires, and intervention manuals) will help others. However, materials are only published after acceptance of the article, so any race has already been won, or lost.

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Competing interests: None declared.

1 Rathi V, Dzara K, Gross CP, Hrynaszkiewicz I, Joffe S, Krumholz HM, et al. Sharing of clinical trial data among trialists: a cross sectional survey. *BMJ* 2012;345:e7570. (20 November.)
2 Ritchie SJ, Wiseman R, French CC. Failing the future: three unsuccessful attempts to replicate Bem's "retroactive facilitation of recall" effect. *PLoS One* 2012;7:e33423.
3 Simmons JP, Nelson LD, Simonsohn U. False-positive psychology: undisclosed flexibility in data collection and analysis allows presenting anything as significant. *Psychol Sci* 2011;22:1359-66.
4 Peters G-JY, Abraham C, Crutzen R. Full disclosure: doing behavioural science necessitates sharing. *Eur Health Psychol* 2012;14:77-84.

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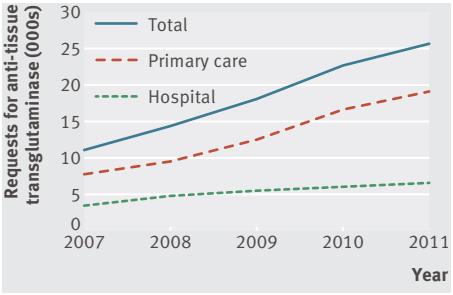
COELIAC DISEASE SEROLOGY

Targeting coeliac disease serology

We agree that testing first degree relatives of patients with coeliac disease (CD) for gluten enteropathy is worthwhile but caution against less targeted testing, especially in patients with non-specific symptoms.[1]



Numbers of requests for anti-tissue transglutaminase in two NHS trusts

The prevalence of CD in England is estimated at 1.0-1.2%.[2 3] Prevalence is higher in "at risk" groups: 5-6% in first degree relatives and 6% in people with type 1 diabetes.[4 5]

We reviewed requests for coeliac serology from two large hospitals and their primary care providers. All sera were tested for anti-tissue transglutaminase antibodies (tTG). Confirming positivity by anti-endomysium antibody testing improves positive predictive values. Berrill and colleagues used IgA anti-tTG alone when reviewing their case,[1] but this test can give false positive results. For primary testing we advise confirmation using the IgA anti-endomysium test.

The figure shows that increasing awareness of CD before the 2009 National Institute for Health and Clinical Excellence (NICE) guidelines resulted in an explosion of requests for serological testing, particularly from primary care. NICE guidance has neither focused testing nor improved yield. Disappointingly, our data suggest that requesting is becoming less effective. Requesting has more than doubled in five years, with the primary care component increasing from 69% to 80% of total requests. The proportion of patients with dual positive serology in primary care has fallen to 1.2% of the tested population.

In this time of austerity patient selection for CD serology needs to be better targeted. In primary care, CD detection is no better than would be achieved by random screening. In the hospital setting (many cases post-GP referral, no doubt) CD detection was highest (around 5%) in children (with failure to thrive, family history, and type 1 diabetes) and in adult diabetes and gastroenterology clinics.

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1 Berrill JW, Ahmed H, Butt S, Swift G. Reviewing a patient with coeliac disease. *BMJ* 2012;344:d8152. (17 January.)
2 Bingley PJ, Williams AJK, Norcross AK, Unsworth DJ, Lock RJ, Ness AR, et al. Undiagnosed coeliac disease at age seven: population based prospective birth cohort study. *BMJ* 2004;328:322-3.
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PRACTICE pp 42, 45; PERSONAL VIEW, p 29

NEUROMUSCULAR DEGENERATION

Understanding absolute versus relative risk reduction

In this Patient's Journey, Mustafa Gunaydin presented to various doctors with marked subjective intolerance of statins before later developing myositis.[1] It seems extraordinary that his doctors were so committed to continued statin treatment. The highest published absolute risk reduction in all cause mortality with statins in secondary prevention of ischaemic heart disease is 3.3% (4S trial[2]), so the number needed to treat is at least 30.[3]

It seems that many doctors are either not aware of the actual benefits of the drugs that they prescribe or do not understand the basic statistical implications of absolute versus relative risk reduction.

Although a population of patients will benefit from full pharmacological secondary prevention in ischaemic heart disease, individual patients should be free to opt out. This patient may have been wise to do so, if a properly informed doctor had counselled him about the actual degree of risk involved.

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Competing interests: None declared.

1 Fisher C, Freris N. Neuromuscular degeneration. *BMJ* 2012;345:e6880. (17 October.)
2 Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383.
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Are statins related to motor neurone disease?

Although it may have been a coincidence that this patient developed motor neurone disease while taking a statin,[1] this also happened to my brother in law.

He was 73 years old and had been taking simvastatin for at least 10 years. Abnormal liver function was attributed to statins, but I do not think creatine kinase was measured until the terminal stages, when it was raised. The diagnosis was missed by at least two doctors. The diagnosis was made by myself and confirmed by a neurologist only three weeks before his death, when he was still driving. As with the account given, he had no weakness of his limbs or of swallowing. All the affected muscles were intercostals, with death being caused by respiratory failure after he developed progressive orthopnoea, which in retrospect had nothing to do with his heart problem. I have seen at least 50 cases of motor neurone disease in my career but have never seen a patient such as this, who presented purely with respiratory failure.

I too thought that the statin may have been a causative factor but could find little in the literature to support this. With widespread use of statins over the past 20 years it would be interesting to see whether the steady increase in death from motor neurone disease is statin related.

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1 Fisher C, Freris N. Neuromuscular degeneration. *BMJ* 2012;345:e6880. (17 October.)

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BMJ'S OPEN LETTER TO ROCHE

Subliminal advertising

This open letter reminded me of a picture I took when I had paused the film *Elf* a couple of years ago during the "stockpiling" of oseltamivir.[1] He was having blood taken for paternity testing. Is this subliminal advertising that families are likely to watch each Christmas?

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1 Godlee F. Open letter to Roche about oseltamivir trial data. *BMJ* 2012;345:e7305. (29 October.)

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