Catheter-directed thrombolysis for acute deep vein thrombosis

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Queen Mary: nobody expects the Spanish Inquisition

Three timely Offline columns by Richard Horton[1–3] describe a mindless managerial rampage spreading through Queen Mary University of London, UK. Barts and The London, Queen Mary's School of Medicine and Dentistry, has declared distinguished medical researchers to be at risk of redundancy.[1] Queen Mary's School of Biological and Chemical Sciences now follows suit.[2,3] As we write, colleagues declared to be "at risk" just 2 weeks ago are summoned individually to closed audiences with the Head of School, attended by members of the ironically named "Human Resources" (HR) department. If targeted individuals fail to appease the inquisitor, they will be sacked. Other staff members are earmarked for demotion, with replacement "Teaching and Scholarship" contracts that will oblige them to desist from independent research.

But, one might ask, is it not high time to weed out slackers? It might help if one had any way of knowing who they are. Sadly, the "restructuring" hits exactly the wrong targets in many cases, and leaves unproductive academics unscathed. The reason is simple—the Head of School and HR have neither interest in, nor understanding of, individuals' research, still less their research potential. This slaughter of the talented relies entirely on a carefully designed set of retrospective counts of the uncountable. These are labelled research "metrics".

Are we here engaged in special pleading? Actually, no.[4] Our school has a reputation, envied worldwide, for research by individuals now for the chop. Their retrospective crimes, committed between 2008 and 2011, include too few publications as a "significant" author in high-impact journals, and below-average external funding. Where the baseline of research income derived from the Higher Education Funding Council for England has disappeared, no-one seems to know. So, we are looking at the end of the road for unique and internationally leading-edge Queen Mary research. Among many outstanding projects we stand to lose are: sociogenomics of mole rats, the only eusocial mammals, and a model, incidentally, for the endocrinology of bullying; genetics of circadian rhythms and iron homoeostasis from experiments on fruit-flies; imaging of neural activity in zebrafish—a paradigm for vertebrate development; and heterogeneous catalytic oxidation and carbon–carbon coupling in inorganic chemical synthesis. The list is long. Alas, there are no boxes to tick for advances in knowledge and understanding—no metrics for science itself.

Over in the Medical and Dental School, the grand inquisitor is identified as the Dean for Research, whose own research credentials are, naturally, unavailable for scrutiny.[1] Never mind, we now have the assurance from his colleague that "Each and every faculty member of the college was assessed in this process and from my own personal point of view it was done fairly…"[5] Who needs evidence in the face of such assurance? "Consequently, to pick him out for criticism in this disgraceful manner is quite iniquitous".[5] Yet the Dean managed to pick out others—for oblivion, not just criticism. And he got it wrong.[1]

The same double standard follows, now, in our School of Biological and Chemical Sciences. For example, one of the "metrics" for research output at professorial level is to have published at least two papers in journals with impact factors of 7 or more. This is ludicrous, of course—a triumph of vanity as sensible as selecting athletes on the basis of their brand of track suit. But let us follow this "metric" for a moment. How does the Head of School fair? Zero, actually. He fails. Just consult Web of Science. Take care though, the result is classified information. HR's "data" are marked Private and Confidential. Some things must be believed. To question them is heresy.

We hope to report back on our Head's one-to-one interview with himself. After all, we have his word, and that of College senior management, that the restructuring is proceeding with complete fairness and transparency. Perhaps he'll use a mirror?

We declare that we have no conflicts of interest.

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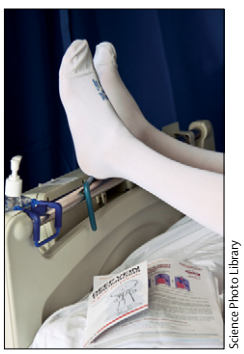
1 Horton R. Offline: Bullying at Barts. *Lancet* 2012; **379:** 1086.
2 Horton R. Offline: Under a tree in Geneva. *Lancet* 2012; **379:** 1182.
3 Horton R. Offline: The bent and twisted. *Lancet* 2012; **379:** 1284.
4 Allen JF. Research and how to promote it in a university. *Future Med Chem* 2012; **2:** 15–20.
5 McDonald S. Bullying at Barts. *Lancet* 2012; **379:** 1483.

Catheter-directed thrombolysis for acute deep vein thrombosis

Tone Enden and colleagues' randomised trial of catheter-directed thrombolysis (CDT) in patients with high proximal deep vein thrombosis (Jan 7, p 31)[1] is well designed and the results have been eagerly awaited. However, we feel that caution is recommended in assigning the 14·4% absolute reduction in the risk of post-thrombotic syndrome in patients on CDT to thrombolysis.

Besides additional treatment, CDT patients were more compliant with wearing compression stockings than were patients who did not receive CDT. Although the difference in compliance of 11·8% is not significant, it is relevant. Daily use of compression stockings reduces the risk of post-thrombotic syndrome by 50%.[2,3] On the basis of this number and



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the incidence of post-thrombotic syndrome in Enden and colleagues' study, we calculate an expected absolute risk reduction in CDT patients of 4%, owing to better compliance with compression stocking use.

Furthermore, more CDT patients than non-CDT patients had good-quality anticoagulant treatment at both follow-up points. Oral anticoagulant treatment that achieves an international normalised ratio within the therapeutic range reduces the risk of post-thrombotic syndrome by 63% compared with patients who spend more than 50% of time beneath the therapeutic range.[4] Unfortunately, time in therapeutic range was not reported in Enden and colleagues' trial and was not accounted for in examining the effect of CDT on post-thrombotic syndrome.

The CDT strategy, with its more intense treatment and hospital admission, does seem to improve outcome. However, this might not be the effect of additional thrombolysis. Instead, it could be due to more intense initial patient support, which results in more awareness of the relevance of treatment compliance. We feel that taking treatment compliance into account is important before coming to conclusions about the effect of thrombolysis on post-thrombotic syndrome and before exposing patients to costly and invasive procedures.

We declare that we have no conflicts of interest.

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1 Enden T, Haig Y, Kløw NE, et al, on behalf of the CaVenT Study Group. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *Lancet* 2012; **379:** 31–38.

2 Brandjes DP, Buller HR, Heijboer H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. *Lancet* 1997; **349:** 759–62.

3 Prandoni P, Lensing AW, Prins MH, et al. Below-knee elastic compression stockings to prevent the post-thrombotic syndrome: a randomized, controlled trial. *Ann Intern Med* 2004; **141:** 249–56.

4 van Dongen CJ, Prandoni P, Frulla M, Marchiori A, Prins MH, Hutten BA. Relation between quality of anticoagulant treatment and the development of the postthrombotic syndrome. *J Thromb Haemost* 2005; **3:** 939–42.

Tone Enden and colleagues, in their CaVenT trial,[1] explore the interesting hypothesis of catheter-directed thrombolysis (CDT) in the prevention of post-thrombotic syndrome. We have several comments.

In the Introduction section, reference to the updated Cochrane review[2] as suggesting a benefit of systemic thrombolysis in prevention of post-thrombotic syndrome comes with the caveat that the only study with a Jadad score of greater than 3 showed no benefit.[3]

The CaVenT trial was done in four specialised centres, and hence the outcomes might be very different elsewhere. Additionally there might have been a learning curve for optimum results with CDT; hence it would be interesting to have a comparison of those who entered the trial earlier versus those who entered later.

Enden and colleagues do not present the bleeding rates (if any) for the control group, and hence a number needed to harm is not available. Also, the rate of stent placement and its association with outcomes would have been interesting, especially in view of scant evidence available on the topic.[4]

The limitations of the open-label design might have manifested with an obvious greater adherence to oral anticoagulation in the CDT group at 6 months. Finally, Enden and colleagues imply a cost effectiveness with CDT, citing the cost associated with post-thrombotic syndrome;[5] however, it would be interesting to assess the expense associated with CDT and other indirect costs associated with the longer hospital stay necessary.

We declare that we have no conflicts of interest.

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1 Enden T, Haig Y, Kløw NE, et al, on behalf of the CaVenT Study Group. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *Lancet* 2012; **379:** 31–38.

2 Watson LI, Armon MP. Thrombolysis for acute deep vein thrombosis. *Cochrane Database Syst Rev* 2004; **4:** CD002783.

3 Arnesen H, Hoiseth A, Ly B. Streptokinase or heparin in the treatment of deep vein thrombosis: follow-up results of a prospective study. *Acta Medica Scand* 1982; **211:** 65–68.

4 Vedantham S. Endovascular procedures in the management of DVT. *Hematology Am Soc Hematol Educ Program* 2011; **2011:** 156–61.

5 Bergqvist D, Jendteg S, Johansen L, Persson U, Odegaard K. Cost of long-term complications of deep venous thrombosis of the lower extremities: an analysis of a defined patient population in Sweden. *Ann Intern Med* 1997; **126:** 454–57.

Authors' reply

Both sets of correspondents raise an issue about whether the noted absolute reduction in post-thrombotic syndrome of 14·4% in patients treated with additional catheter-directed thrombolysis (CDT) could be attributed to the thrombolytic treatment alone, since a higher proportion of these patients reported daily wear of elastic compression stockings and had international normalised ratios within the therapeutic range.

We agree that the non-significant tendency to better compliance could be attributable to the inherent risk of bias of this open-label randomised controlled trial, and relevance to the noted effect size cannot be ruled out. However, we think the effect on post-thrombotic syndrome cannot be simplified as suggested by Inge van Schouwenburg and colleagues. First, the two landmark studies on the use of elastic compression stockings[1,2] reported on patients with any level of proximal deep vein thrombosis (DVT) from the popliteal vein and up, whereas our patients had a high proximal