NICE guidance on reducing the risk of venous thromboembolism in patients admitted to hospital

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DECLARATIONS

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The clinical guideline on the prevention of venous thromboembolism (VTE) applicable to all hospital patients was published by the National Institute for Health and Clinical Excellence (NICE) in January 2010¹ with considerable media attention. We believe that adherence to this guidance will save lives that might otherwise be lost due to preventable pulmonary embolism (PE). After the guideline launch, NICE and the Chair of Guideline Development Group (GDG) received many e-mails from doctors and members of the public including everything from extremely well-argued and robust challenges, through common misconceptions, to highly individualized personal perspectives. We are prompted by some recurring themes, or what might be called 'frequently asked questions', to address some of these issues.

The clinical guideline recommends that the first step is that all patients should be assessed at or before hospital admission. This involves a 'checklist'. The checklist approach has been found to save lives when applied to surgical operations² and yet it is met with resistance and scorn by some doctors.³ Who would be impressed to discover that the airline pilot had skipped the preflight checklist because he found it a bore? There is safety for the majority in a checklist – otherwise, while concentrating, quite rightly, on the immediate clinical problems of the particular medical admission or surgical operation we might forget important elements of the background safety drills. In the case of hospital-acquired VTE and its prevention, the checklist has been developed in collaboration between GDG and the Chief Medical Officer's Working Group and will be implemented with the backing of the Department of Health.

The checklist is designed to be inclusive so that opting out of VTE prophylaxis should be a con-

scious decision. Any tick against VTE risk prompts reference to the NICE clinical guideline. Some of our e-mails came from doctors who describe a patient in whom slavish adherence to guidelines would seem to them illogical. A guideline is there to guide not dictate; it cannot be made to fit 100% of situations. Finding a loophole in the guideline does not discredit it in its entirety. The checklist should be implemented in 100% of admissions but clinical exclusion resulting in, for example, 90% compliance might well be about right. Health professionals should use good sense and clinical judgement in applying guidance to individual patients – but be prepared to defend a decision not to follow it.

A problem with clinical judgement is that a recent memorable disaster tips the balance. Powerful evidence for this effect was found in the not dissimilar clinical question of anticoagulation of patients in atrial fibrillation to reduce the risk of stroke.^{4,5} If one of their patients had a bleed, doctors were less likely to prescribe anticoagulants in subsequent patients; a single event in their recent experience weighed more heavily than the total published evidence. But perhaps worse, if an untreated patient had a stroke, no alteration in practice occurred. So, altering practice on the basis of experience is not even-handed: errors of commission weigh more heavily than errors of omission. The background to the VTE guidance is the reported common failure to prevent death due to PE.⁶ VTE prophylaxis with anticoagulants is not 100% effective and is not 100% safe. That is why all risks are carefully considered by the GDG and their consequences weighed in terms of QALYs lost and gained. The guideline attempts to find the nadir of risk for all our patients rather than the individual comfort zone of doctors.

Figure 1

There is generally accepted to be a continuum between asymptomatic DVT and fatal PE, with a common underlying pathological cause. We have used Heinrich's triangle to illustrate this. If the commoner events at the triangle's base are reduced then there is a commensurate reduction in fatal PE.⁷

We have been asked specifically why we did not include children with inflammatory bowel disease, patients with cancer on the waiting list, and why a relative's life was not saved after admission to hospital with a PE. Our answer to all of these questions, and many others like them is that they are outside our 'scope'. The frame or boundaries within which we offer guidance are determined at the beginning of the process and governs the search for evidence which may include many thousands of papers, and after exclusion of many in the case of VTE, over 400 randomized controlled trials (RCTs) remained for analysis. Each of these was critically appraised and meta-analysed and health economic models constructed for the particular setting. So the apparently simple matters of defining a hospital admission and how to categorize a day-case have to be agreed by the GDG. Others might have made other choices but the decisions were not reached without much deliberation.

There are other working decisions that had to be made at the outset. If you come into hospital for the

common elective operations such as cholecystectomy or hip replacement, a PE is the most likely thing to kill you. Are we entitled to use risk reductions from RCTs where the outcome was asymptomatic DVT to inform strategies to reduce deaths due to PE? If not, we severely curtail the evidence base. Fatal PE occurs at a statistically low rate and trials powered with PE as an endpoint would require many tens of thousands of patients. A form of common cause hypothesis⁷ is generally agreed for VTE and has been the premise of teaching and practice for years (Figure 1). Thus, asymptomatic DVT, PE, and death due to PE event rates have a reasonably stable ratio one to another. Does this always apply? Does it apply to knee surgery for instance? It is arguable that local surgical causes may increase the rate for detectable DVT in knee surgery which do not share a common cause with fatal PE and then the ratio breaks down. The question can only be resolved by gaining and interpreting the evidence. We may need more.

Not all settings have been studied. The largest part of the evidence is in surgical patients and most of that is in general surgery and orthopaedics. An ENT surgeon correctly points out that there is no direct evidence that applies to his practice. But there are biological triggers related to surgery and the degree of reduced mobility entailed for its performance and recovery which have a degree of commonality. Either the GDG generalizes the available evidence on VTE risk and its modification, or offers no guidance at all for a very large number of patients having operations for which evidence was not specifically acquired. A doctor can still make a clinical judgement to deviate from guidance for an individual patient, but it would be wise to document this decision, with the reason.

Extrapolation from one setting to another is itself a judgement. In one instance, the GDG had to modify guidance at the 11th hour when faced with new evidence in the use of graduated compression stockings. The existing evidence was that stockings reduced risk of VTE by about 50% based on studies in surgical patients. Furthermore, mechanical methods are without risk of bleeding and so their use seemed a reasonable first resort in patients for whom there is clinical concern about even a small bleeding risk, such as those with stroke. Then the CLOTS study reported that in patients admitted with stroke, there was no reduction in VTE risk with thigh-length stockings versus no

Figure 2

General surgery: outcome DVT. Network meta-analysis constructed so that indirect comparisons can be made. For example fondaparinux was only compared with the then 'best' existing agent, low molecular weight heparin. VKA: vitamin K antagonists; Asp: aspirin; GCS: graduated compression stockings; UFH: unfractionated heparin; LMWH: low molecular weight heparin; IPCD; intermittent pneumatic compression device; Fon: fondaparinux

stockings and a small but definite burden of harm related to skin pressure.⁸ In the face of this direct evidence against them, we could not recommend stockings for patients with stroke. But what did this evidence do for other extrapolations? Should the new CLOTS evidence be applied in non-stroke medical patients or should we use the evidence gained in surgical patients? This was not straightforward and was discussed at length by the GDG and a consensus reached. We wonder what others would have done?

There are other gaps in direct evidence. More recently introduced drugs have never been examined in a placebo-controlled trial. In RCTs they have been compared with the best existing drugs. To overcome this limitation, an ingenious and mathematically sophisticated method of incorpo-

rating all RCT evidence and without breaking randomization has been developed, called network meta-analysis (Figure 2).⁹ Readers of guidance should be mindful of the amount of work and level of sophistication that goes into NICE guideline development, particularly if the guidance is at odds with their previous practice. The opinions of individual doctors on a case-by-case basis are not a satisfactory way of preventing VTE. It is not possible to compute, on the basis of experience, the relative numerical risks of VTE versus bleeding; both events occur too infrequently and there are too many other variables. Furthermore, decisions made on the basis of experience respond to recent events and discount remote events. It is a clinical question for which the NICE method of careful evaluation of all available evidence is at its most useful and we believe has clear advantages over known alternatives.

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