LETTERS

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NHS SERVICE TO PRIVATE PROVIDER

Circle commits to working with NHS on service transformation

Iacobucci's article noted that Circle has provided a good dermatology service in Nottingham, but it missed three crucial facts.[1]

Firstly, dermatologists employed by Nottingham University Hospitals (NUH) have been working for Circle since 2008 and were required to transfer employment to us only in 2013, thanks to a change in national law.

Secondly, the independent review noted that dermatology staff who transferred thought that Circle is a good, empowering employer and would encourage colleagues to think again about Circle.

Finally, for context, four dermatologists chose not to transfer to us. One subsequently came to work for us anyway. Across the entire hospital, 119 NUH staff chose to transfer.

These facts all point to the same conclusion: this is not simply about working for private partnerships like Circle.

The independent review makes it clear that the solution is for all the main parties to work closely together, and Circle fully commits to collaboration with NUH and commissioners on securing services.

The issue at stake, though, is one being faced across the NHS and across different specialties. Demand is going up, the workforce is not always expanding at the same pace, and funding is tight. Alongside increasing the number of training places, part of the answer has to be service transformation, involving better use of technology, self care, using trained nurse and GP specialists, and better diagnosis. Circle's approach has been to try to lead that transformation, and our firm belief is that only strong clinical input can create sufficiently imaginative solutions.

The example of Nottingham shows that leadership is needed for the NHS to navigate a challenging time, and that will be most powerful when it is driven by clinicians.

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1 Iacobucci G. Transfer of services from NHS to private provider was "unmitigated disaster," report says. *BMJ* 2015;350:h3161. (9 June.)

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SEPSIS IN CHILDREN

Review on sepsis in children did not mention important trial

I wonder why Plunkett and Tong did not discuss the FEAST trial in their review of sepsis in children.[1 2] This trial of fluid boluses in African children with severe infection was controversial, both for its results and inclusion criteria.[3] But it seems a huge oversight not to mention the only randomised controlled trial on fluid boluses in sepsis, especially when a recent systematic review supported its weight,[4] and the authors disagree with its conclusions.

Might the authors explain why this trial was not discussed?

I am aware that this is an educational review, so clear instructions and advice on management are needed, but that is no excuse for not mentioning what is arguably the most important trial in paediatric sepsis in the past decade.

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1 Plunkett A, Tong J. Sepsis in children. *BMJ* 2015;350:h3017. (9 June.)

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"Paedatric sepsis six" requires further validation

Plunkett and Tong advocate using the "paediatric sepsis six" in the management of children with sepsis.[1] This is stated to be an operational tool designed to improve adherence to national guidelines. However, given that it includes advice on diagnosis and recognition of sepsis it is also likely to be viewed as a clinical decision tool to help identify sepsis in children.

Unfortunately, the diagnostic criteria in this tool are so broad that a considerable number of children would probably be overtreated if it was widely adopted. Around 20% of children attending the emergency department have a fever.[2] Only 7% of these will have a serious bacterial illness and not all will require intravenous antibiotics.[3] There is no clear consensus on the predictive value of single vital signs such as heart rate or capillary refill time in identifying sepsis,[4] but the paediatric sepsis six gives these factors central importance. If this tool was widely adopted, many more children might therefore receive intravenous antibiotics and fluids than need to.

Diagnosing sepsis in febrile children is a key challenge for paediatricians. It is difficult to distinguish between the few who will benefit from intravenous antibiotics and the many who will not. There is currently no evidence that the paediatric sepsis six improves outcomes in children with sepsis, but it may lead to overtreatment—it should therefore be validated in more clinical settings before being widely implemented.

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Authors' reply

Hamilton highlights an important topic of debate regarding sepsis management in children.[1 2] The study he mentions was a well conducted trial with robust outcome data and we do not disagree with its conclusions. We decided not to discuss this trial because the case selection and context of a randomised controlled trial constrain the applicability of the results. The FEAST investigators studied children with septic shock, without severe hypotension, in a resource limited setting.[3] Nevertheless, the trial does raise an important general question regarding liberal versus restrictive fluid resuscitation of children with severe sepsis and septic shock. Further evidence is likely to be forthcoming in this area soon, and we also await with interest the National Institute for Health and Care Excellence guideline on intravenous fluid therapy in children, the draft of which is available for consultation now.

King worries that the use of Paediatric Sepsis 6 (PS6) risks overtreatment of sepsis.[4] He clearly explains his reasons for concern

and we agree with the referenced data. However, he may have overlooked two features of PS6. Firstly, PS6 contains nothing that is not found in existing national and international guidance. Secondly, as clearly stated in PS6, when using this tool, the decision to diagnose sepsis is entirely down to the clinician. This last point is a unique feature, which differentiates PS6 from any form of algorithmic diagnosis making tool.

The question of validation is interesting and we welcome debate in this area. No data on the use of PS6 have been published, although we expect reports to be published soon. The validity of the clinical diagnosis of sepsis will be influenced by multiple factors, including the experience of attending clinicians.

Our clinical review highlighted the importance of early recognition and treatment of sepsis in children. PS6 prompts clinicians to use clinical judgment to consider sepsis in children who may benefit from rapid treatment and offers a simplified and structured approach based on the best available evidence and consensus.

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PFIZER AND PREGABALIN

Pregabalin is only partially effective for neuropathic pain

As a patient with knowledge about research and development (R&D), and marketing, receipt of a prescription for generic pregabalin for neuropathic pain prompted a call to my GP about a possible error. Initially she blamed the pharmacist but the prescription did not specify indication. Subsequent prescriptions have been for Lyrica.

Professionally I am fully aware of escalating R&D costs and maximising patent life.[1] However, as a patient, pregabalin is only partially effective in dulling neuropathic pain, with dose dependent debilitating side effects; albeit better than gabapentin. The problem is the lack of effective drugs for neuropathic pain.

Pfizer also uses a flat pricing structure. Trying to save NHS money, I avoid one capsule three times a day and take one twice a day, saving 30%.

I believe there are now fewer different capsule concentrations, making it harder to optimise doses and reduce side effects, especially when concomitant drugs kick in temporarily.

Pfizer's income from Lyrica for neuropathic pain is increasing, partly because of improved

diagnosis and life expectancy, increased symptoms related to spondylitis, and more operations that can damage nerves.

Is Pfizer reinvesting any of these "unexpected" profits in researching more effective drugs for neuropathic pain? If so, apologies might be accepted by all. If not, maybe Pfizer should review its pricing strategy for an already expensive drug used chronically and invest less in its legal battles to lengthen this patent.

Lyrica was Pfizer's highest generator of income/profit in 2014, with growth in developed countries for neuropathic pain.[2] Investment in a sustained release product may be useful to patients and patent life, but would depend on trial outcome and pricing.

Finally, shareholders should understand their profits will never return to the levels of three decades ago and will probably drop further, especially with expensive "niche" drugs dominating R&D.

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1 Jack A. Pfizer steps up battle to defend control of pregabalin. *BMJ* 2015;350:h3119. (8 June.)

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HYPERCALCAEMIA

Problems with the diagnostic algorithm for hypercalcaemia

The diagnostic algorithm in Minisola and colleagues' excellent review of hypercalcaemia contains several debateable points.[1]

Firstly, the authors suggest confirming hypercalcaemia after vitamin D supplements are discontinued, but high vitamin D rarely contributes to hypercalcaemia if supplementation is not excessive. Directly proceeding to calcidiol measurements provides more certainty and avoids unnecessary delays.

The authors then suggest calcidiol supplements if levels are <50 nmol/L in patients with hypercalcaemia and unsuppressed parathyroid hormone. However, this has no relevance to diagnosis because low vitamin D is common in the most likely cause of these findings (primary hyperparathyroidism), and this doesn't require normal vitamin D levels to establish the diagnosis in cases of clear hypercalcaemia.

Thirdly, they suggest that hypercalcaemia in the presence of a glomerular filtration rate <60 mL/min/1.73 m^2 can be attributed to hypocalciuria in chronic kidney disease (CKD). However, hypercalcaemia usually occurs only after prolonged and much more severe CKD (<15 mL/min/1.73 m^2), and is usually caused by adynamic bone disease, vitamin D analogues, excess calcium carbonate, tertiary hyperparathyroidism, or transplantation. The authors' suggested cut off is far too high, and might result in many elderly patients in primary care whose hypercalcaemia is caused by primary hyperparathyroidism inappropriately being classified as having just CKD.

Finally, the authors mention hypermagnesaemia in familial hypocalciuric hypercalcaemia but do not discuss hypomagnesaemia that occurs secondary to primary hyperparathyroidism, which can aggravate some symptoms of hypercalcaemia. In my opinion, serum magnesium values have diagnostic and therapeutic consequences in patients with unsuppressed parathyroid hormone and therefore constitute an integral part of the diagnostic and management approach at that point.

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1 Minisola S, Pepe J, Piemonte S, et al. The diagnosis and management of hypercalcaemia. *BMJ* 2015;350:h2723. (2 June.)

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Authors' reply

We agree with Laurent's first two points, even though hypovitaminosis D may cause hypocalciuria, raising the doubt of familial hypocalciuria hypercalcemia.[1 2] There is much debate around the issue of vitamin D in patients with primary hyperparathyroidism[3 4]; we believe that calcidiol should be measured because vitamin D insufficiency worsens skeletal involvement, for example.

Regarding the third point, we were referring to hypocalciuria and not hypercalcaemia. The thresholds reported are those set for the distinction between primary hyperparathyroidism and familial hypocalciuria hypercalcaemia, an important step to avoid unnecessary operations.

The role of magnesium is important, but because of space limitations we did not mention it.[5]

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