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## Fast track referral for cancer

Moyez Jiwa and Christobel Saunders

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## Editorials

### Fast track referral for cancer

*Has not improved patient outcomes in the UK*

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In formulating such rules, it is important to remember that waiting times for urgent appointments are only a surrogate end point. The main aim is to improve cancer survival, improve psychosocial outcomes for people with cancer and those who turn out not to have cancer, and to improve the general practitioner's ability to diagnose cancer. This rule seems not to have led to any of these outcomes, although it has perhaps increased the proportion of patients with benign pathology referred for urgent specialist appointments.

Introduction of the two week standard clinics has not improved the outcomes for patients in some of the commonest cancers.<sup>2</sup> The reason for this may be the complexity of the medical consultation. Many factors affect the decision to refer for an expert opinion, including a patient's help seeking behaviour, doctor-patient communication, eliciting and interpreting signs and symptoms, applying evidence to decision making, negotiation with the patient about the need for and most appropriate route of referral, and conveying the information in sufficient detail to allow the patient to be fully informed about the need for urgency or otherwise. It has been calculated that if the practitioner successfully negotiates each of the above stages on 80% of occasions then only a small percentage of decisions will be evidence based.<sup>3</sup>

A substantial proportion of patients with common cancers present as emergencies with advanced disease; in the case of colorectal cancer this has been estimated to be as high as 20%.<sup>4</sup> This is especially true in deprived communities or in communities where people have cultural and linguistic differences.

A major step towards earlier diagnosis of cancer would be to raise awareness of the symptoms of cancer in the community. Furthermore, given that cancer is an uncommon diagnosis in general practice, practitioners are unlikely in most cases to opt to investigate symptomatic patients.<sup>5</sup> Therefore patients with altered bowel habit may not be tested for iron deficiency anaemia or other signs of occult bleeding as symptoms are far more likely to be due to irritable bowel syndrome or diverticular disease than to colorectal cancer.<sup>6</sup>

Bayes's theorem demonstrates that the probability that a patient has cancer is affected by the prevalence. The prevalence of cancer in a primary care population depends on the symptoms in question. Such considerations should influence the selection of patients for referral.<sup>7</sup> In practice, however, doctors will act on the basis of personal experience, respected local opinion, and anecdotal evidence rather than on high quality published research.<sup>8</sup> Research about the positive predictive value of signs and symptoms of the common cancers in primary care does exist. Implementing these findings in practice, however, will require substantial effort.<sup>9 10</sup>

General practitioners must also be able to persuade patients with suspicious symptoms that a specialist opinion is required. In practice, however, it is the patients with worrisome symptoms of benign pathology who are likely to demand an urgent specialist appointment. Given that cancers also present with symptoms associated with benign conditions and in view of the rising tide of litigation and complaint from patients sensitised to sensational stories of misdiagnosis, it is hardly surprising that patients are being inappropriately referred through the fast track route.<sup>11</sup> This phenomenon can also be

explained by Braess's paradox, whereby "adding extra capacity to a network, when the moving entities selfishly choose their route, can in some cases reduce overall performance" ([http://en.wikipedia.org/wiki/Braess'\\_paradox](http://en.wikipedia.org/wiki/Braess'_paradox)).

So what is the best strategy for deciding which patients to refer for specialist opinion? Maybe one day we will have a reliable and valid test to help identify cancer patients in primary care. Until then, general practitioners should make a provisional diagnosis on the basis of a history and a physical examination, paying particular attention to genetic predisposition, exposure to carcinogens, and the type and duration of symptoms. Effective lines of communication between general practitioners and cancer specialists or networks will help to relay these clinical details, leading to earlier and more accurate diagnosis. Technological innovations that facilitate this process without being intrusive or cumbersome in practice may be more successful than published guidelines or schemes to ration urgent appointments only to those with a limited list of signs and symptoms.

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## References

1. Potter S, Govindarajulu S, Shere M, Braddon F, Curran G, Greenwood R, et al. Referral patterns, cancer diagnoses, and waiting times after introduction of two week wait rule for breast cancer: prospective cohort study. *BMJ* 2007;335:288-90. doi: 10.1136/bmj.39258.688553.55[Abstract/Free Full Text]
2. Flashman K, O'Leary DP, Senapati A, Thompson MR. The Department of Health's "two week standard" for bowel cancer: is it working? *Gut* 2004;53:387-91.[Abstract/Free Full Text]
3. Glasziou P, Haynes B. The paths from research to improved health outcomes. *Evid Based Med* 2005;10:4-7. [Free Full Text]
4. Chohan DP, Goodwin K, Wilkinson S, Miller R, Hall NR. How has the "two-week wait" rule affected the presentation of colorectal cancer? *Colorectal Dis* 2005;7:450-3.[CrossRef][ISI][Medline]
5. Hamilton W, Sharp D. Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Fam Pract* 2004;21:99-106.[Abstract/Free Full Text]
6. Jiwa M, Burr J. GP letter writing in colorectal cancer—a qualitative study. *Current Medical Research & Opinion* 2002;18:342-6.[CrossRef]
7. Summerton N. Making a diagnosis in primary care: symptoms and context. *Br J Gen Pract* 2004;54:570-1.[ISI][Medline]
8. Gabbay J, le May A. Evidence based guidelines or collectively constructed "mindlines?" Ethnographic study of knowledge management in primary care. *BMJ* 2004;329:1013.[Abstract/Free Full Text]
9. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax* 2005;60:1059-65.[Abstract/Free Full Text]
10. Hamilton W, Round A, Sharp D, Peters TJ. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *Br J Cancer* 2005;93:399-405.[CrossRef][ISI][Medline]
11. Hurwitz B. Learning from primary care malpractice: past, present and future. *Qual Saf Health Care* 2004;13(2):90-1.[Free Full Text]

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## EDITORIALS

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Has not improved patient outcomes in the UK



#### RESEARCH, p 288

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- 9 Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax* 2005;60:1059-65.
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## Are health services in England failing our children?

Poor outcomes for major childhood diseases reflect the low status of children's NHS services

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In 2004, the UK government launched the national service framework for children in England.<sup>1</sup> It contained a comprehensive set of standards for children's health services and a 10 year timescale for implementation. The framework was welcomed as the first real blueprint for children's health since the Court Report<sup>2</sup> almost 30 years before. But with no extra money and no specific targets for health professionals or managers, progress has been slow. Children have been given a low priority, and managers are distracted by high profile government targets for emergency waiting times and surgical waiting lists. There is now real concern and increasing evidence that the National Health Service (NHS) is failing children.

The Healthcare Commission recently produced "Improving services for children in hospital,"<sup>3</sup> a review of progress on national service framework standards in England. In 2006, only 4% of trusts were rated excellent and 21% were rated good. While the commission reported considerable progress in improving the hospital environment for children, their review noted a worrying potential for unsafe medical care. Surgeons trained to operate on adults were operating on children, many on only a handful each year. In a small number of NHS trusts too few trained staff were available to provide effective life support for children during the day. One in five trusts was unable to deal effectively with paediatric emergencies at night.

Children in England with diseases such as diabetes and cancer generally do badly, when compared with their peers in the rest of Europe. We have, for example, one of the highest incidences of type 1 diabetes and one of the worst records on diabetic control.<sup>4</sup> This could be linked to differences in lifestyle and diet, but poor services are probably at least partly to blame.<sup>5</sup> Good diabetic control is vitally important for children because we know that late complications of diabetes in adult life are determined by what happens in childhood. Our inadequate children's services are inevitably storing up

problems for the future and we can avoid them only by investing in better care now. Unfortunately, "short termism" has so far prevailed.

The picture is similar for children with cancer. According to recent estimates, children with cancer in Britain have a five year survival rate of 71%, compared with 77% for Scandinavian children and 75% for children elsewhere in western Europe (France, Germany, Netherlands, and Switzerland).<sup>6</sup> British children possibly wait longer for diagnosis and referral to specialists. In Germany, for example, more than 27% of Wilms's tumours are picked up by routine health surveillance by primary care paediatricians.<sup>7</sup> This compares with less than 10% in the United Kingdom, where surveillance has been slimmed down, is largely done by nurses, and does not include abdominal palpation at regular intervals. Many office paediatricians in Germany have their own ultrasound machines and are trained to use them.

Our care of newborns also gives cause for concern. The Department of Health has recently reviewed the public services agreement target on health inequalities and infant mortality. The target aims by 2010 to reduce by at least 10% the gap in infant mortality between the socioeconomic class labelled the "routine and manual occupational group" and the English population as a whole.<sup>8</sup> The NHS is falling behind in efforts to improve this important indicator of care during the antenatal and perinatal periods, and in the first year of life. England now lies 15th in the European league table for perinatal mortality. Much hope was built around the establishment in 2004 of neonatal networks of care—linked professional groups working across primary, secondary, and tertiary care to ensure equitable and clinically effective services—these have proved hard to establish and coordinate in the real world without adequate national direction and funding.<sup>9</sup>

All is not lost, however. For example, there have been substantial improvements in community child and adolescent mental health services during the past

three years, facilitated by ring fenced additional funding and proxy targets (which serve as indicators that the 10 year plan is on track) for delivering comprehensive services. Recent reports from the Paediatric Surgical Forum,<sup>10</sup> the Department of Health,<sup>11</sup> and the Royal Colleges<sup>12</sup> suggest ways to improve the provision of surgical services for children, and also to improve emergency care and ensure children's safety. A report out this week highlights the difficulties of providing general paediatric surgery in the district general hospital and suggests ways that this might be tackled.<sup>13</sup> Networks of well trained staff with appropriate skills and competencies are central to all these efforts.<sup>13</sup>

Reconfiguration of services is also essential, problems must be resolved with the tariff for specialist paediatric services through "Payment by results" (the system by which providers are paid from a fixed tariff for each individual case treated in NHS hospitals), and true partnerships of care through managed clinical networks (groups of healthcare professionals working across boundaries to provide comprehensive care for particular conditions) need to be established for all major acute and long term childhood illnesses. Above all, children's health must be taken more seriously. It is an investment for the future that we cannot afford to get wrong.

1 Department of Health. National service framework for children, young people and maternity services. London: Department of Health, 2004. [www.dh.gov.uk/en/PolicyAndGuidance/HealthAndSocialCareTopics/ChildrenServices/ChildrenServicesInformation/DH\\_4089111](http://www.dh.gov.uk/en/PolicyAndGuidance/HealthAndSocialCareTopics/ChildrenServices/ChildrenServicesInformation/DH_4089111).

- 2 Court SDM. *Fit for the future. The report of the committee on child health services*. London: HMSO, 1976.
- 3 Healthcare Commission. *Improving services for children in hospital*. London: HC, 2007. [www.healthcarecommission.org.uk/\\_db/\\_documents/children\\_improving\\_services\\_Tagged.pdf](http://www.healthcarecommission.org.uk/_db/_documents/children_improving_services_Tagged.pdf).
- 4 Danne T, Mortensen HB, Hougaard P, Lynggaard H, Aanstoot HJ, Chiorelli F, et al. Persistent differences among centers over 3 years in glycemic control and hypoglycemia in a study of 3805 children and adolescents with type 1 diabetes from the Hvidovre Study Group. *Diabetes Care* 2001;24:1342-7.
- 5 Department of Health. *Making every young person with diabetes matter*. London: DoH, 2007. [www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_073674](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_073674).
- 6 Steliarova-Foucher E, Coebergh JW, Kaatsch P, Pritchard Jones K, Stillier C. Cancer in children and adolescents in Europe. *Eur J Cancer* 2006;42:1913-2190.
- 7 Graf N, Reinhard H, Aliani S, Engelmann D, Leuschner I, Semler O. Wilms' tumour with or without tumour related symptoms at diagnosis abstract. *Med Pediatr Oncol* 2003;41:266.
- 8 Department of Health. *Review of health inequalities infant mortality PSA target*. London: DoH, 2007. [www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_065544](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_065544).
- 9 Marlow N, Gill AB. Establishing neonatal networks: the reality. *Arch Dis Child* 2007;92:F137-42.
- 10 Association of Paediatric Anaesthetists, Association of Surgeons for Great Britain and Ireland, British Association of Paediatric Surgeons, Royal College of Paediatrics and Child Health, Senate of Surgery for Great Britain and Ireland. *Joint statement: surgery*. 2006. [www.rcpch.ac.uk/doc.aspx?id\\_Resource=1777](http://www.rcpch.ac.uk/doc.aspx?id_Resource=1777).
- 11 Department of Health. *The acutely or critically sick or injured child in the district general hospital; a team response*. [www.dh.gov.uk/en/Consultations/Closedconsultations/DH\\_4124412](http://www.dh.gov.uk/en/Consultations/Closedconsultations/DH_4124412).
- 12 Intercollegiate Committee for Services for Children in Emergency Departments. *Services for children in emergency departments*. Royal College of Paediatrics and Child Health, 2007. [www.rcpch.ac.uk/doc.aspx?id\\_Resource=2626](http://www.rcpch.ac.uk/doc.aspx?id_Resource=2626).
- 13 Children's Surgical Forum. *Surgery for children: delivering a first class service*. London: Royal College of Surgeons of England, 2007. [www.rcseng.ac.uk](http://www.rcseng.ac.uk).

## Neglected tropical diseases

These diseases could be controlled or eliminated in our lifetimes if efforts are better coordinated

In 2002 one of us wrote an editorial in the *BMJ* entitled "The world's most neglected diseases," referring to 13 ancient tropical infections of the poor (box).<sup>1</sup> These diseases are disabling, disfiguring, and stigmatising; they impair children's physical and cognitive growth; they promote poverty; and many of the drugs used to treat them are toxic, difficult to administer, and are more than 50 years old.<sup>2</sup> Five years ago, there was little good news to report. But recently there has been a silent revolution in the attention being paid to these diseases.<sup>2</sup> We see several reasons for optimism.

Firstly, the long held belief that it is not economically feasible to develop drugs, diagnostic methods, and vaccines specifically for the neglected tropical diseases has now been shattered.<sup>4</sup> Although these conditions exclusively affect the world's poorest people, product development partnerships have been established for at least six neglected tropical diseases in the past seven years without commercial markets or conventional business models, and several new drugs and vaccines are in the pipeline.<sup>5,6</sup>

This increase in drug development activity is not a passing trend. Moran and colleagues surveyed the

landscape of drug development for neglected tropical diseases and found that 63 drug projects were under way at the end of 2004 (although some of these were for malaria and tuberculosis, diseases that are not considered to be among the most neglected).<sup>4</sup> On the basis

### Main neglected tropical diseases

#### Protozoan infections

Human African trypanosomiasis

Visceral leishmaniasis

Chagas disease

#### Helminth infections

Soil transmitted helminths

hookworm, ascariasis, trichuriasis

Schistosomiasis

Lymphatic filariasis

Onchocerciasis

Dracunculiasis

#### Bacterial infections

Trachoma

Leprosy

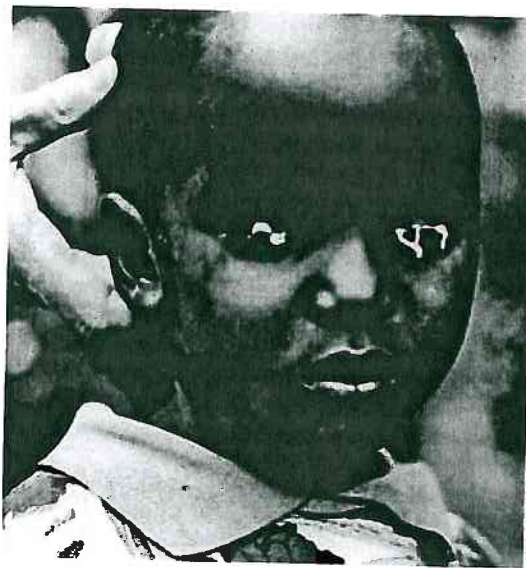
Buruli ulcer

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JASON KELVIN/SPL

of standard attrition rates, and assuming ongoing funding, we can expect to see eight or nine new drugs for neglected tropical diseases within the next five years. This increased pharmaceutical activity by public-private partnerships is now being complemented by the development capabilities of the so called “innovative developing countries,” such as Brazil, India, and China.<sup>7</sup> These countries have spent decades building infrastructures for developing their own drugs, vaccines, and diagnostics, with minimal financial or technical help from the rich world.

Furthermore, the moral duty to scale up use of the existing tools for controlling neglected diseases is becoming clearer. “A scientist who is also a human being,” said Albert B Sabin, who developed the oral polio vaccine, “cannot rest while knowledge which might reduce suffering rests on the shelf.” For some of the neglected tropical diseases, the current drugs, if administered to everyone at risk, could certainly reduce suffering. Indeed, the World Health Assembly’s targets for controlling five of the neglected tropical diseases (lymphatic filariasis, onchocerciasis, trachoma, soil transmitted helminth diseases, and schistosomiasis) emphasise mass drug administration. The African programme for onchocerciasis control is a good example—by the end of this year, treatment with ivermectin will have reached 65 million people ([www.worldbank.org/afr/gper](http://www.worldbank.org/afr/gper)).

Given that the neglected tropical diseases often occur in the same geographical areas, and given evidence that a drug used by one disease specific vertical programme could simultaneously affect other diseases, there is now great interest in rolling out an integrated package of disease control. For example, a package of four drugs (albendazole, ivermectin, azithromycin, and praziquantel) could integrate the control of seven major neglected tropical diseases for 500 million people in Africa and could be delivered for about \$50 (£25; €36) per person each year.<sup>2</sup> Furthermore, tackling neglected parasitic diseases could enhance the effectiveness of antiretroviral therapy in endemic regions.<sup>8</sup>

The penny has finally dropped among donors—they have realised that because chronic parasitic diseases leave people mired in poverty, controlling these diseases will help to achieve the Millennium Development Goal of halving the proportion of people living on less than a dollar a day by 2015 ([www.undp.org/mdg/](http://www.undp.org/mdg/)). Lymphatic filariasis, for example, is responsible for the loss of 0.63% of India’s gross national product,<sup>9</sup> while the global annual loss of productivity related to impaired vision and blindness from trachoma is as high as \$5.3bn.<sup>10</sup>

The United States Agency for International Development has recently awarded a \$100m grant to scale up integrated control of neglected diseases in Africa.<sup>11</sup> This amount, however, is still less than 10% of the funds needed in sub-Saharan Africa alone for widescale implementation of interventions for neglected tropical diseases.<sup>12</sup>

One problem facing the community working on controlling neglected tropical diseases is the lack of communication between the various players—researchers, policy makers, clinicians, public-private partnerships, donors, and patient advocacy groups. Finally, we have an online tool for such communication—the world’s first journal specifically devoted to these diseases. The Bill and Melinda Gates Foundation has awarded the Public Library of Science a grant of \$1.1m to launch in October 2007 *PLoS Neglected Tropical Diseases* ([www.plosntds.org](http://www.plosntds.org)), an open access, non-profit journal. One unusual feature of the journal is that, unlike other tropical medicine journals,<sup>13</sup> 40% of the editors who handle peer review are from countries where the neglected tropical diseases are endemic.

- 1 Yamey G. The world’s most neglected diseases. *BMJ* 2002;325:176-7.
- 2 Molyneux DH, Hotez PJ, Fenwick A. “Rapid-impact interventions”: how a policy of integrated control for Africa’s neglected tropical diseases could benefit the poor. *PLoS Med* 2005;2:e336.
- 3 PLoS Medicine Editors. A new era of hope for the world’s most neglected diseases. *PLoS Med* 2005;2:e323.
- 4 Moran M, Ropars A-L, Guzman J, Diaz J, Garrison C. *The new landscape of neglected disease drug development*. London: Wellcome Trust, 2005.
- 5 Renslo AR, McKerrow JH. Drug discovery and development for neglected parasitic diseases. *Nat Chem Biol* 2006;2:701-12.
- 6 Hotez PJ, Ferris MT. The antipoverty vaccines. *Vaccine* 2006;24:5787-99.
- 7 Morel C, Broun D, Dangi A, Elias C, Gardner C, Gupta RK, et al. Health innovation in developing countries to address diseases of the poor. *Innovation Strategy Today* 2005;1:1-15. <http://www.biodevelopments.org/innovation/index.htm>.
- 8 Gallagher M, Malhotra I, Mungai PL, Wamachi AN, Kioko JM, Ouma JH, et al. The effects of maternal helminth and malaria infections on mother-to-child HIV transmission. *AIDS* 2005;19:1849-55.
- 9 Nutman TB. Lymphatic filariasis: new insights and prospects for control. *Curr Opin Infect Dis* 2001;14:539-46.
- 10 Frick KD, Hanson CL, Jacobson GA. Global burden of trachoma and economics of the disease. *Am J Trop Med Hyg* 2003;69:1-10.
- 11 Control of Neglected Tropical Diseases Project. *Control of neglected tropical diseases*. USAID, 2006. [www.usaid.gov/our\\_work/global\\_health/id/ntd\\_brief.pdf](http://www.usaid.gov/our_work/global_health/id/ntd_brief.pdf).
- 12 Fenwick A, Molyneux D, Nantulya V. Achieving the Millennium Development Goals. *Lancet* 2005;365:1029-30.
- 13 Keiser J, Utzinger J, Tanner M, Singer BH. Representation of authors and editors from countries with different human development indexes in the leading literature on tropical medicine: survey of current evidence. *BMJ* 2004;328:1229-32.