the Responsibility Deal—eg, the need for robust, independent, transparent scrutiny of commitments made and the benefits of a local approach.

Public health sits within a wider socioeconomic system. The project was developed to operate at this scale by a public health team in the region that was prepared to take a risk with an unproven concept.[4] Critics need to accept that insufficient evidence that an intervention is meeting planned outcomes because of short follow-up times does not equal evidence that such initiatives do not work. The scepticism with which projects of this nature have been met suggests a partisan view made on preformed conclusions rather than objective evidence. A reconsideration of this stance is in order.

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1 Horton R. Offline: Where is public health leadership in England? *Lancet* 2011; **378:** 1060.
2 Department of Health. Public Health Responsibility Deal. http://www.dh.gov.uk/en/Publichealth/Publichealthresponsibilitydeal/index.htm (accessed June 28, 2011).
3 Emphas!s. East Midlands Platform on Obesity, Physical Activity and Health. http://www.emphasisnetwork.org.uk/regionalplatform.htm (accessed Sept 13, 2011).
4 Wanless D. Securing good health for the whole population: final report—February 2004. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4074426 (accessed Nov 1, 2011).

Hydroxycarbamide use in young children with sickle-cell anaemia

The report by Winfred Wang and colleagues (May 14, p 1663)[1] provides encouraging results from the safety studies of the use of hydroxycarbamides in young children. However, the conclusion that these agents can now be used in all children with sickle-cell anaemia might be premature, since there are still several unanswered questions.

First, given the current knowledge about disease phenotypes, it is not clear that the sample size in this study captured a fair representation of severe disease phenotypes. Thus whether the safety profile of this drug will justify its use in all or a select group of young infants with sickle-cell anaemia remains an open question.

Second, and perhaps more important, is the need to address the potential use of this drug where it is likely to have the most effect on global health—ie, settings with a high prevalence of sickle-cell anaemia and poor health-care infrastructure. What is the potential effect of long-term neutropenia and hyposplenism on the outcome of patients in settings where malaria is endemic and invasive bacterial infections are highly prevalent? Will the hydroxycarbamides in these settings reduce the need for frequent blood transfusions where safe blood transfusion cannot be readily guaranteed? The genotoxic and teratogenic potentials of this drug require more data.

Now is also the appropriate time to initiate dialogue with the manufacturers of this drug, international donor agencies, and national governments in the sub-Saharan region to ensure easy access, once safety and efficacy is proven in that region.

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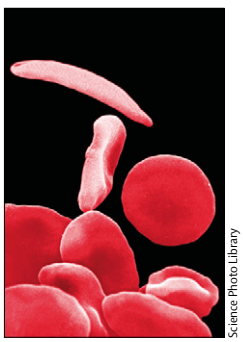
1 Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle-cell anaemia: a multicentre, randomised, controlled trial (BABY HUG). *Lancet* 2011; **377:** 1663–71.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Winfred Wang and colleagues[1] report that hydroxycarbamide therapy can now be considered for all very young children with sickle-cell anaemia, whether or not they have clinical symptoms. However, secondary cancer is a substantial concern in patients who receive long-term hydroxycarbamide.[2] Complications and clinical efficacies must be balanced. In Wang and colleagues' trial, some patients were asymptomatic, and the severity of the underlying disease varied widely between patients. Whether early initiation of hydroxycarbamide is beneficial in asymptomatic patients as well as those with severe sickle-cell anaemia remains unknown.

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1 Wang WC, Ware RE, Miller ST, et al. Hydroxycarbamide in very young children with sickle cell anaemia: a multicentre, randomised, controlled trial (BABY HUG). *Lancet* 2011; **377:** 1663–72.
2 Schultz WH, Ware RE. Malignancy in patients with sickle cell disease. *Am J Hematol* 2003; **74:** 249–53.

Need to realign patient-oriented and commercial and academic research

Clinical research is motivated by several factors. Some are more defensible than others, but most clinical researchers would state that their research is intended to improve health-care effectiveness and safety. There are examples where patients have succeeded in influencing what gets studied,[1,2] but these are exceptions.

I have had the opportunity to consider from more than one perspective the mismatch between

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what clinical researchers do and what patients need. I am a researcher; I have responsibility for allocating funding for research; and I have had multiple myeloma for the past decade. A few years ago I stated publicly that several uncertainties I faced at the beginning of my disease were avoidable.[3] Almost 10 years later—after a relapse of my disease—I looked at the "epidemiology" of myeloma studies on ClinicalTrials.gov. On July 31, 2011, a search using the term "multiple myeloma" identified 1384 studies. Of these, 107 were phase 2/3 comparative studies. However, in only 58 of these studies was overall survival an endpoint, and in only ten of these was it the primary endpoint. No trial was a head-to-head comparison of different drugs or strategies. Meanwhile, experts feel that cytogenetic studies and gene-expression profiling will lead to personalised treatment in myeloma,[4] and pharmaceutical companies avoid research that might show that new and expensive drugs are no better than another comparator already on the market.

If we want more relevant information to become available, a new research governance strategy is needed. Left to themselves, researchers cannot be expected to address the current mismatch. Researchers are trapped by their own internal competing interests—professional and academic—which lead them to compete for pharmaceutical industry funding for early-phase trials instead of becoming champions of strategic, head-to-head, phase 3 studies.

Nor are patients' groups alone likely to change the prevailing pattern of research: given the lack of explicit mechanisms for research prioritisation, they are often dominated by experts with vested interests. Neither would public funding alone solve the problem.[5] Policies developed in the preapproval phase of drug development are needed, and this process needs strict collaboration with pharmaceutical companies and with input from regulatory bodies.

An essential component of any new governance strategy would be to bring together all the stakeholders, starting from an analysis of existing and ongoing research, produced independently of vested interests. Patient advocacy groups in myeloma spend millions to support research, hoping to promote better care. With public support they should be in a strong position to call for a redefinition of the research agenda, in the interests of patients. I hope this approach can be further debated in *The Lancet* for many other areas of clinical research in oncology and beyond.

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1 Buckley BS, Grant A, Glazener CMA. Case study: a patient-clinician collaboration that identified and prioritized evidence gaps and stimulated research involvement. *J Clin Epidemiol* 2011; published online Aug 3. DOI:10.1016/j.jclinepi.2011.03.016.

2 Stewart RJ, Caird J, Oliver K, Oliver S. Patients' and clinicians' research priorities. *Health Expect* 2010; published online Dec 22. DOI:10.1111/j.1369-7625.2010.00648.x.

3 Liberati A. An unfinished trip through the uncertainties. *BMJ* 2004; **328:** 531–32.

4 Russel SJ, Rajkumar SV. Multiple myeloma and the road for personalised medicine. *Lancet Oncol* 2011; **12:** 617–19.

5 Liberati A, Moja PL, Trotta F, Traversa G. Feasibility and challenge of independent research on drugs: the Italian Medicines Agency (AIFA) experience. *Eur J Clin Invest* 2010; **40:** 69–86.

Department of Error

Usher AD. Donors continue to hold back support from the Global Fund. Lancet *2011;* **378:** *471–72*—In this World Report (Aug 6), the first line of the seventh paragraph should have read "Germany, the Global Fund's fourth largest donor after the USA, France, and the UK, immediately froze its disbursement of $285 million that had been allocated for 2011". The correction has been made to the online version as of Nov 18, 2011.

The Lancet. China's major health challenge: control of chronic diseases. Lancet *2011;* **378:** *457*—In this Editorial (Aug 6), the first sentence of the second paragraph should have read "A headline statistic in the report is that reduction of mortality from cardiovascular disease by only 1% per year between 2010 and 2040 will save the country a staggering US$10·7 trillion…" This correction has been made to the online version as of Nov 18, 2011.

Mandell DS, Levy SE, Schultz RT. Effectiveness of intensive autism programmes—Authors' reply. Lancet *2010;* **375:** *723*—In this Correspondence (Feb 27, 2010), the second paragraph should have read: "With regard to other randomised trials of ABA, space limitations prevented a more thorough listing of references within that review; however, referenced within Rogers and Vismara's article is Rogers's 1998 review[3] of five studies preceding the five referenced in her 2008 article. We originally classified these as randomised trials, but accept that they in fact involve closely matched (but not randomised) comparison groups." This correction has been made to the online version as of Nov 18, 2011.

Malfertheiner P, Bazzoli F, Delchier JC, et al. Helicobacter pylori *eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial.* Lancet *2011;* **377:** *905–13*—In this Article (March 12), the fourth sentence of the third paragraph in the Procedures section (p 906) should have read: "In the 7-day standard regimen, one capsule of omeprazole, two of amoxicillin, and one of clarithromycin were taken twice daily (before morning and evening meals)." This correction has been made to the online version as of Nov 18, 2011.

Wang YC, McPherson K, Marsh T, et al. Health and economic burden of the projected obesity trends in the USA and the UK. Lancet *2011;* **378:** *815–25*—In this Series paper (Aug 27), the x-axes of parts A–D of figure 5 were labelled incorrectly. The label should have been x100 000, and the values should have been different for the USA (10, 20, 30) and the UK (2, 4, 6). These corrections have been made to the online version as of Nov 18, 2011.