in cured individuals, but it is also quite possible that drug-induced reduction (and not necessarily eradication) of the parasite load could be sufficient to arrest the evolution of the disease and avert its irreversible long-term consequences. Moreover, even if one admits that the seroconversion rate after antitrypanosomal treatment in the late chronic phase is quite low (let’s say 10%), for every 10 patients treated, one will be cured, and thousands of infected individuals could derive some clinical benefit from a 60-day course of treatment. Of note, few therapeutic interventions in medicine have such a favourable number needed to treat.

In the "small" trial mentioned by Victor Issa and Edimar Bocchi, 566 chronically infected adults were enrolled. After a median follow-up of 9.8 years, fewer treated patients had progression of disease (hazard ratio 0.24, 95% CI 0.10–0.59; p=0.002) on chronic Chagas heart disease. If the result is positive, the recommendations for trypanocidal therapy in this specific situation should move to class I (always indicated). If it is negative, to class III (not recommended).

We declare that we have no conflicts of interest.

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The International Study of Insulin and Cancer

Studies have suggested the possibility of an association between use of insulin glargine and cancer, with conflicting results. Among other issues under debate is the role of insulin itself in cancer development and the contribution of confounding factors or analytical methods to observations. The International Study of Insulin and Cancer (ISICA) is an effort to address thoroughly the association of breast cancer with insulin use. ISICA has received an unrestricted grant from Sanofi-Aventis and has been reviewed by the European Medicines Agency.

Using case-control methods, the ISICA study aims mainly to assess the association of breast cancer with the use of individual insulins such as the analogues glargine, lispro, and aspart, and human insulin formulations such as isophane and regular human insulin, compared with non-insulin use in patients with diabetes. Analysis will account for mitigating or risk factors such as oral antidiabetes agents (specially metformin), type of diabetes, gestational diabetes, life-time body-mass index, reproduction-related factors, oral contraceptives, hormone replacement therapy, cancer in first-degree relatives, socioeconomic status, and behavioural risk (alcohol, smoking), among others. Also, several biological variables will be assessed (eg, HER2, oestrone, or progesterone receptors, and circulating insulin).

A registry of 12 500 patients with breast cancer, diagnosed with a first positive biopsy between January, 2008, and June, 2009 (ie, before the cited publications), will be identified through pathology records and medical charts by a network of at least 50 centres across the UK, France, and Canada that treat at least 100 breast cancer patients per year. Cases, defined as those who also have diabetes, will be identified. At least 1000 of such patients are expected to meet this criterion and 750 will be included. Eligible patients will be female, at least 18 years old, without previous history of breast cancer, and willing and able to participate. Controls will be patients with diabetes who fulfil the same eligibility criteria and who are free of cancer at the time of matching to cases. Controls will be independently recruited from general medical practices. An average of four controls will probably be matched to each case on type of diabetes, age, country, and region, totalling 3000 controls.
Exposure to insulin and other drugs will be collected from patients’ general practitioners or pharmacy records. All patients will be interviewed for individual risk factors and blood samples will be collected and tested for biological markers. Data and blood samples will be available to various researchers. Descriptive analysis and multivariable modelling will be done for case-control comparisons. The study results are expected in mid-2012.

The ISICA group: M Blettner, Y Ohashi, J A Extra, L Mignot, F Penalou-Llorca, D Rea, A Thompson, W Weller. LGB’s institution (LA-SER) was paid by Sanofi-Aventis to independently conduct the study. MM has received consultancy fees from Sanofi-Aventis, Debiopharma, and Celgene; payment for development of educational presentations including service on speakers’ bureaux from Roche and AstraZeneca; and reimbursement of travel or accommodation expenses from Sanofi-Aventis. MP has received consultancy fees or honoraria for work on ISICA from La-Ser and Sanofi-Aventis, and consultancy fees, grants, and travel expenses for other work from Novo Nordisk, Sanofi-Aventis, and Pfizer. DC received consulting fees and travel expenses during the design stage of ISICA from Sanofi-Aventis. MR has received honoraria for consulting and for chairing a consulting group regarding insulin glargine, as well as research grants, speakers’ fees, and travel grants from Sanofi-Aventis. BC has received fees for consultancy, advisory boards, speaking, travel, or accommodation from Takeda, GlaxoSmithKline, Merck Sharpe & Dohme, AstraZeneca, Bristol-Myers Squibb, Boehinger Ingelheim, Novo Nordisk, Roche, Sanofi-Aventis, and Novartis. AHB has received honoraria for advisory work and lectures unrelated to this work from Sanofi-Aventis, Eli Lilly, and Novo Nordisk. PB’s institution has received a grant for a study on glargine and cancer, and PB has received honoraria for advisory board meetings from Sanofi-Aventis. JFB has been a scientific advisory board member for Sanofi-Aventis and received reimbursement for travel to board meetings. ME has received grants and consultancy fees from Eli Lilly, Novo Nordisk, and Sanofi-Aventis. MR has received honoraria for advisory work and lectures unrelated to this work from Sanofi-Aventis, Eli Lilly, and Novo Nordisk. JB has no conflicts of interest. LA’s institution (LA-SER) received an unrestricted grant from Sanofi-Aventis for the ICISA study. LA is a stock owner and chairman of LA-SER and has received speakers’ fees, payment for manuscript preparation, and has stock options in AstraZeneca, Boiron, Expanscience, Genevieve, GSK, Janssen-Cilag, Merck/Shering Plough, Neuma/Wokhardt, Novartis, Pfizer, and several divisions of Sanofi. He was also a former Chief Medical Officer in France (1999–2003), and has taken decisions on almost all the drugs reimbursed during that period, including some studied during the ISICA study.

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Cause-of-death data to support MDG 4 progress

Cause-of-death data, as presented by Robert Black and colleagues (June 5, p 1969), will be important in guiding intervention priorities to reach Millennium Development Goal 4 (MDG 4; to reduce mortality in children younger than 5 years by two-thirds between 1990 and 2015). India accounts for 21% of global deaths in children younger than 5 years; 54% of these deaths occur in the neonatal period. Two further steps are needed, however, to improve performance of countries that are currently unlikely to meet MDG 4, such as India. First, high mortality regions and social groups within countries need to be prioritised. In several rural, underserved areas inhabited by tribal communities in Orissa and Jharkhand, the neonatal mortality rate is the same as the Indian national average was 30 years ago (about 60 per 1000 livebirths). Second, disaggregated cause-of-death data, at the subnational level and by socioeconomic group, are essential. Regions and groups with high mortality levels probably show quite different cause-of-death patterns to the national average, leading to different intervention priorities.

Low-cost mortality surveillance systems are feasible, even in poor, rural states, and among tribal populations. In our study sites, we monitor births and deaths in half a million people in tribal Orissa and Jharkhand, and do verbal autopsies for all maternal and neonatal deaths. Replication of this approach in other high-mortality settings, perhaps through sentinel sites, would generate data to allow policy makers to prioritise appropriate interventions for high-mortality regions and social groups, and would enhance global efforts to achieve MDG 4.

All authors are involved in running low-cost mortality surveillance systems in study sites in Orissa and Jharkhand, India. TH, AC, and AP are also involved in mortality surveillance sites in Bangladesh, Nepal, and Malawi.

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