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Expanded HIV screening in the US is cost-effective

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Two articles published in *The New England Journal of Medicine* last February indicated that a broader screening for HIV in the US could offer health care benefits at a reasonable cost. Such issues have not been addressed in the new era of highly active antiretroviral therapy (HAART).

Current approach is failing

Since 2003 the Centers of Disease Control and Prevention (CDC) recommend routine HIV counselling and referral in settings with at least a 1% prevalence for HIV. But what happens in practice differs from the recommendation. Despite this initiative, an estimated 280,000 Americans are still unaware of their HIV infection. Voluntary HIV tests should be recommended more routinely in health care settings, but they are not. 'We know from other studies that people find out late in the course of their HIV infection, when they are almost to AIDS or already have AIDS,' said Douglas Owens, author of one of two articles. 'We know that the current approach is failing,' he added.

Owens, from the Department of Veterans Affairs, Palo Alto Health Care System and at Stanford University, Stanford, California, together with first author Sanders and colleagues, have developed a decision model to estimate the health benefits and expenditures of performing voluntary HIV screening [1]. In the other article [2], Paltiel from Yale University in Connecticut and his colleagues developed a computer simulation model of HIV screening and treatment to predict the costs and benefits of HIV counselling, testing and referral in three target groups: 'high risk' (3% prevalence of undiagnosed HIV infection; 'CDC threshold' (1% prevalence) and 'US general' (0.1% prevalence).

Health care benefits of screening

Paltiel and co-workers' estimated that the addition of one-time screening for HIV would raise the average CD4 count at the detection of HIV infection from 154 to 210 cells per cubic millimeter and that the proportion of cases diagnosed at a late stage would drop. Earlier access to treatment should make the suppression of viral replication easier, improve immunity and reduce drug-related adverse effects. Both studies concluded that the effect of screening would extend survival by 1.5 years for the average HIV-infected patient.

Health care benefits of expanded HIV screening would have a reasonable cost. 'When we say that routine screening for HIV is cost-effective, we are not saying that early screening will save money. The cost-effectiveness of early HIV screening means that it will confer to people more health benefit per dollar spent', commented Paltiel.

In populations with a prevalence of HIV of 1% or greater, both studies estimated that the cost of one-time screening is around $40,000 per quality-adjusted life-year gained. This is less than the commonly cited threshold for cost-effective care of $50,000 per quality-adjusted life-year gained. Cost-effectiveness changes with the prevalence of disease: Paltiel's group found that in the general US population, which has a 0.1% prevalence of HIV infection, the costs would increase to $113,000 per quality-adjusted life-year gained.

'The benefit of screening will be to individuals but also to the general population by reducing transmission', said Owens. His group estimated that routine one-time screening would reduce the annual rate of transmission by slightly more than 20%.

New screening guidelines

How can HIV testing be increased in practice? 'First, we hope that screening guidelines will change and take these new data into account. Second, we hope that HIV screening will become a routine part of care, voluntary of course, even for groups with a prevalence lower than 1%', said Owens. 'The fact that 81% of adults in the United States see health care providers at least once a year should be exploited', added Paltiel. But how many of

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those individuals will accept an HIV test? 'We don't know', said Paltiel. 'But we know that the methods for screening and counselling are critical', added Owens. ' We know for instance that with the traditional methods of screening, a good proportion of people never pick up their results. Rapid tests would be of a great interest to these individuals, since they would get their results quicker'.

'These findings are in line with what the CDC recommended two years ago,' commented Karlie Stanton, spokesperson at the CDC. 'We certainly will take these studies into account in our next HIV testing guidelines', she added. The models do not incorporate certain negative effects of screening. 'We are aware that our analysis does not consider stigma, a critical concern in shaping public perception of HIV', said Paltiel. Acceptance of testing and linkage to care represent a second area for study. 'In addition, we don't really know who will pay for these tests', said Paltiel.

Would these models be applicable to developing African and Asian countries for instance, where HIV kills the most? 'Our study is based on US standards of care and linkage to care', said Paltiel. 'The value of earlier detection is based on the state of the art HAART, the lab facilities allowing to tailor HAART to each individual and the possibility to interfere with further transmission on the disease. 'We are currently working on models applicable to Asian and African countries'. 'Benefit occurs if care is available,' said Owens. 'There is no point testing people if there is no treatment available. Obviously getting treatment to people is absolutely urgent', he added.

References

1 Sanders, G.D. *et al.* (2005) Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *New Engl. J. Med.* 352, 570–585
2 Paltiel, A.D. *et al.* (2005) Expanded screening for HIV in the United States – an analysis of cost-effectiveness. *New Engl. J. Med.* 352, 586–595

New leukemia drug shows promise against Gleevec resistance

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Patients with chronic myelogenous leukemia (CML) resistant to Gleevec, the most successful treatment for the deadly cancer, could have a promising alternative drug in the future, according to early studies by US researchers. CML is caused by the Philadelphia chromosome, an abnormality that produces the BCR-ABL cancer protein. Gleevec works by binding to BCR-ABL and completely blocking its activity, thereby stopping cancer growth.

Synergy

'Our drug [ON012380] works just like Gleevec but by blocking another part of the BCR-ABL protein. It can be combined with Gleevec to create synergy and when patients become resistant to Gleevec, our drug kills 100% of the cancer cells', said lead researcher, Prem Gumireddy, Director of the Fels Institute for Cancer Research at Temple University School of Medicine.

The implication of this study is that clinicians will soon have combination therapies to improve the treatment of CML, said Paul Travers, deputy director of the leukemia charity Anthony Nolan Trust. 'There are other drugs in the pipeline that also target BCR-ABL and which are active against most of the Gleevec-resistant variants but this compound can act synergistically with Gleevec, while the others cannot', said Travers.

Resistance

About 750 people per year in the UK have advanced CML and a small number develop Gleevec resistance within a few years of starting therapy. The actual number of patients who develop resistance depends on the stage of the disease and their previous treatment, said Ken Campbell clinical information officer at the Leukaemia Research Fund. 'In patients put on Gleevec as first-line therapy in the early chronic phase, it is probably no higher than 10%. But in late-stage disease it may be quite high', said Campbell. Currently the alternatives for patients who develop resistance are either to use 'older' drugs alone or in combination or to

temporarily withdraw Gleevec, which may restore sensitivity, said Campbell.

However, Richard Sullivan, Head of Clinical Programmes at Cancer Research UK, said there are likely to be a number of mutations and other mechanisms that cause resistance. 'Doctors would have to genotype resistant patients to see which of many second-line treatments might help them. Screening genes in this way is not straightforward, and may hamper the future use of compounds such as ON012380', he warned. The study was published in the early online edition of *Proceedings of the National Academy of Sciences* [1].

New challenge

Until now scientists have only managed to develop two experimental drugs that could tackle some but not all forms of Gleevec resistance CML. However, both drugs failed to block the activity of a mutant BCR-ABL, called T315I, a more predominant mutation in Gleevec-resistant patients.

When developing their drug, Reddy and colleagues targeted parts of the BCR-ABL protein that didn't appear to be mutating and adapting to Gleevec.

As a result, in human tumour cell and mouse model experiments, the compound called ON012380 induced cell death of all of the known Gleevec-resistant mutants and caused regression of leukemias, said Reddy, who is currently seeking FDA approval to proceed with clinical trials

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