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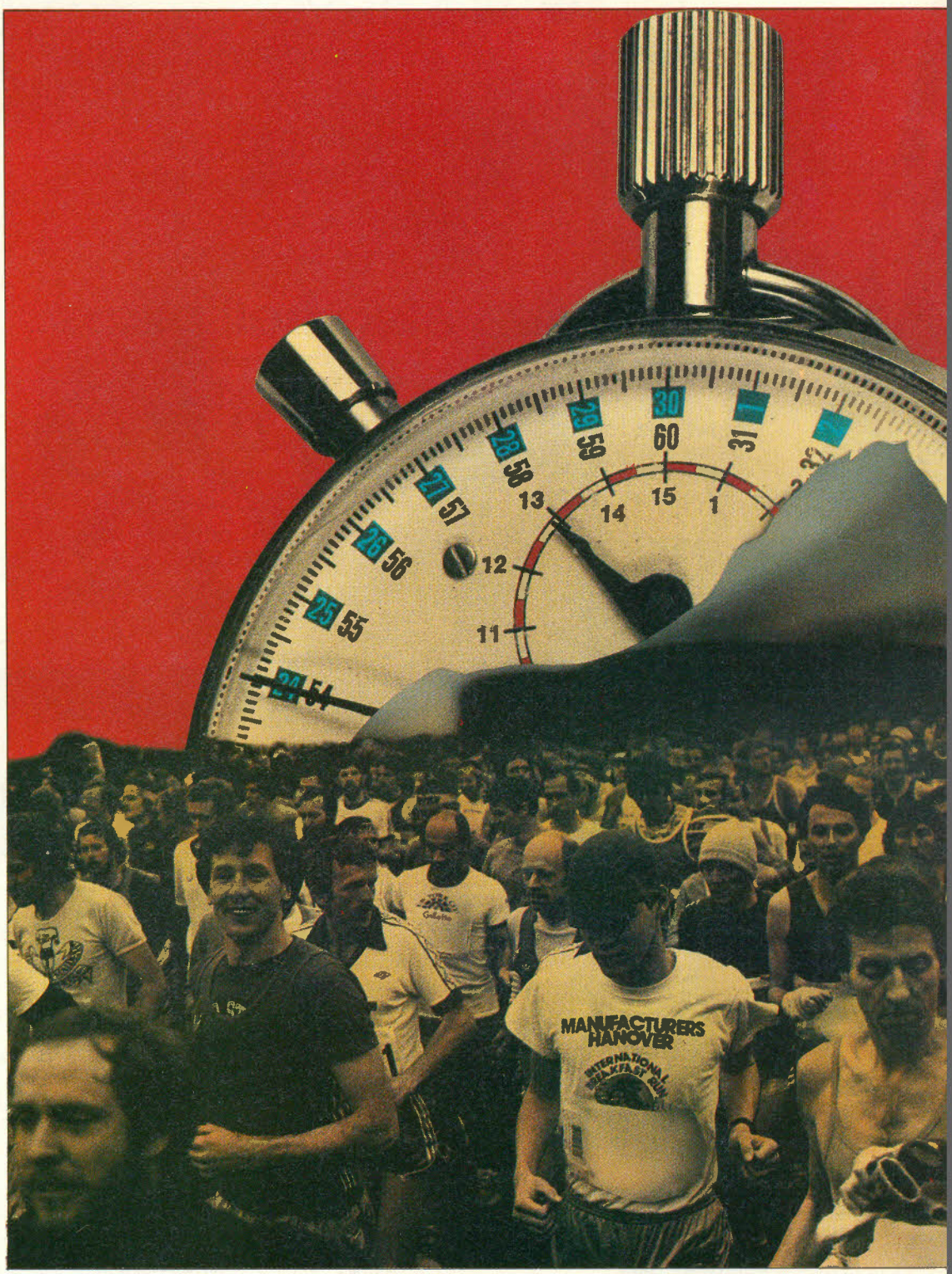


Aids can't be cured—but it can be stopped. If the government invests in research *now* it could save 50,000 lives and £20 billion. But as Duncan Campbell reports, it's hardly started

Race against Time

Aids: the race against time

A cure for Aids is probably ten years away. Vaccines are even further off. But there is already a way to stop people dying of the disease, by slowing down the rate at which HIV develops into full-blown Aids. "Early intervention" in Britain could save up to 50,000 lives and £20 billion. The trouble is, reports Duncan Campbell, that the government has put scarcely a penny into the necessary research.

In a tightly-packed clinic in London's Fitzrovia, Dr Ian Weller and his colleagues chart every week the fate of 300 courageous young men involved in an epic tragedy. He has known most of the 300 personally, for almost six years. Since 1982—when his hospital, the Middlesex, began preliminary studies on the nature of Aids—they have become his acquaintances and friends. By the end of 1988, about 60 of these originally healthy young men had died. Most of the rest are ill.

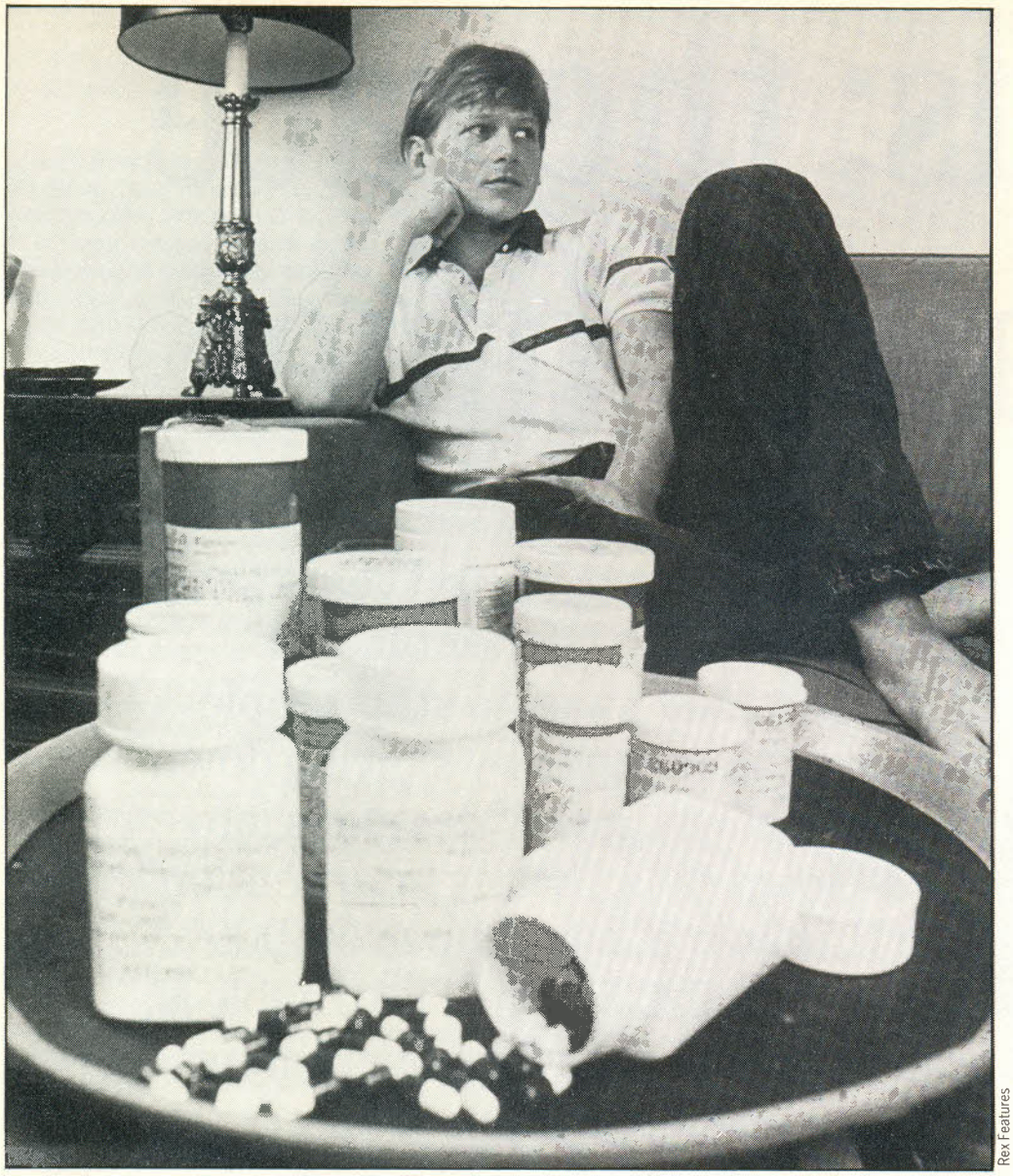
Weller's chart is a kaleidoscope of coloured squares, one for each person. The colour denotes their status—white for healthy, green if they have symptoms of Aids. "When I began, that chart was white," says Weller. "It's almost a lawn now, with just a few bare patches." The bare patches represent those who have not yet progressed to clinical disease or premature death.

Once, Weller and other practitioners could sincerely tell patients infected with HIV that "most" people infected didn't get ill. The chart—and time itself—has now taught him and his patients a different and painful story. "We can't keep people's heads in the sand any longer," he says. So what was once a *de facto* medical secret, for the best of reasons—the belief that HIV infection was probably always going to lead to Aids—is now out in the open. The grim predictions of "progression" to clinical disease are now too widely known.

In this way, time has come to seem the greatest enemy of those affected by Aids or HIV, or who are trying to provide a medical response. But research based on the latest developments in the United States has shown that Aids' seemingly nastiest weapon—the long time it takes to incubate—can be turned against it. Analysis based on the latest projections of Aids for Britain shows that more than 90 per cent of the future death toll can be avoided if the right research is begun now and implemented quickly.

But time is of the essence; with HIV, it is a desperate race against time.

Last month, the Department of Health's working party on the short-term prediction of Aids, chaired by Sir David Cox, produced the first comprehensive assessment of the levels of Aids in England and Wales into the early 1990s. Cox and his colleagues estimated that at least



Rex Features

30,000 fewer people could develop Aids by the year 2000 with early treatment for HIV

20,000 to 50,000 people were now infected by HIV, and that 8,000 or more new cases of Aids would therefore arise before the end of 1992.

What their report did not point out is that, without therapeutic intervention, *all* those already infected—plus anyone newly infected in 1988 and subsequent years—will probably also go on to suffer and die from "full-blown" Aids. That means between 16,000 and 50,000 more deaths than Cox predicted for 1992.

With a death toll like that, it is not just health care costs and personal suffering that will be heavy. The economic cost of Aids is greatly magnified by the age and gender grouping of the potential casualties, including a high proportion of economically active young males, for whom decades of productive life are at risk. Such deaths impose a disproportionately high economic loss on the whole nation.

In Britain, health care costs alone are estimated now to be approaching an average of £30,000 per person between diagnosis and death. (About £80 million a year is already being spent by the Department of Health on treating Aids and HIV infection.) Similar costs of about $57,000 per head (£32,000) have been incurred in the United States. But the impact on the health system in the US is many times more severe. In New York City, where almost 18,000 Aids cases have now been diagnosed, bed capacity in major public hospitals has been completely exhausted.

The overall economic costs of Aids to the US have also been calculated. The average present value of lost production from each Aids death is estimated to have been $600,000 in 1987, rising to $800,000 in 1991. By then, according to health economist Dr Anne Scitovsky of the University of California, San Francisco, the further cost of the 144,000 people then predicted to have contracted Aids will be $77.5 billion. Even this may only be 10 to 20 per cent of the potential US Aids and HIV disease death toll. If the larger of the estimates of the extent of HIV infection in America produced by the US Centers for Disease Control proves correct, and medical intervention is late or ineffectual, then the eventual economic cost of Aids to the United States could easily exceed *one thousand billion dollars*.

In Britain, the cost of failing to curb Aids and HIV disease will be somewhere between £5 and £20 billion, quite apart from the loss of 20,000 to 50,000 people, mostly now in their 20s and 30s. If the full extent of present and future HIV infection has been underestimated, or continues to grow, then the ultimate potential death toll and loss to the British economy will be that much larger. Although these figures may seem astronomic, it is worth noting that the total cost of Aids to the US economy already stands at $8.7 billion, of which $7 billion is the net loss of economic production from those now dead or dying from Aids.

So far, four paths are being followed to end the Aids epidemic. Three of them will either fail in the short term, or are so far insufficient to curb deaths from Aids.

- *Education* measures are directed against the means by which HIV is transmitted, usually aiming at modifying people's behaviour (usually sexual behaviour).

- *Cures* for full-blown Aids are being urgently researched—but nothing which is clearly effective is yet in the drugs-testing pipeline.

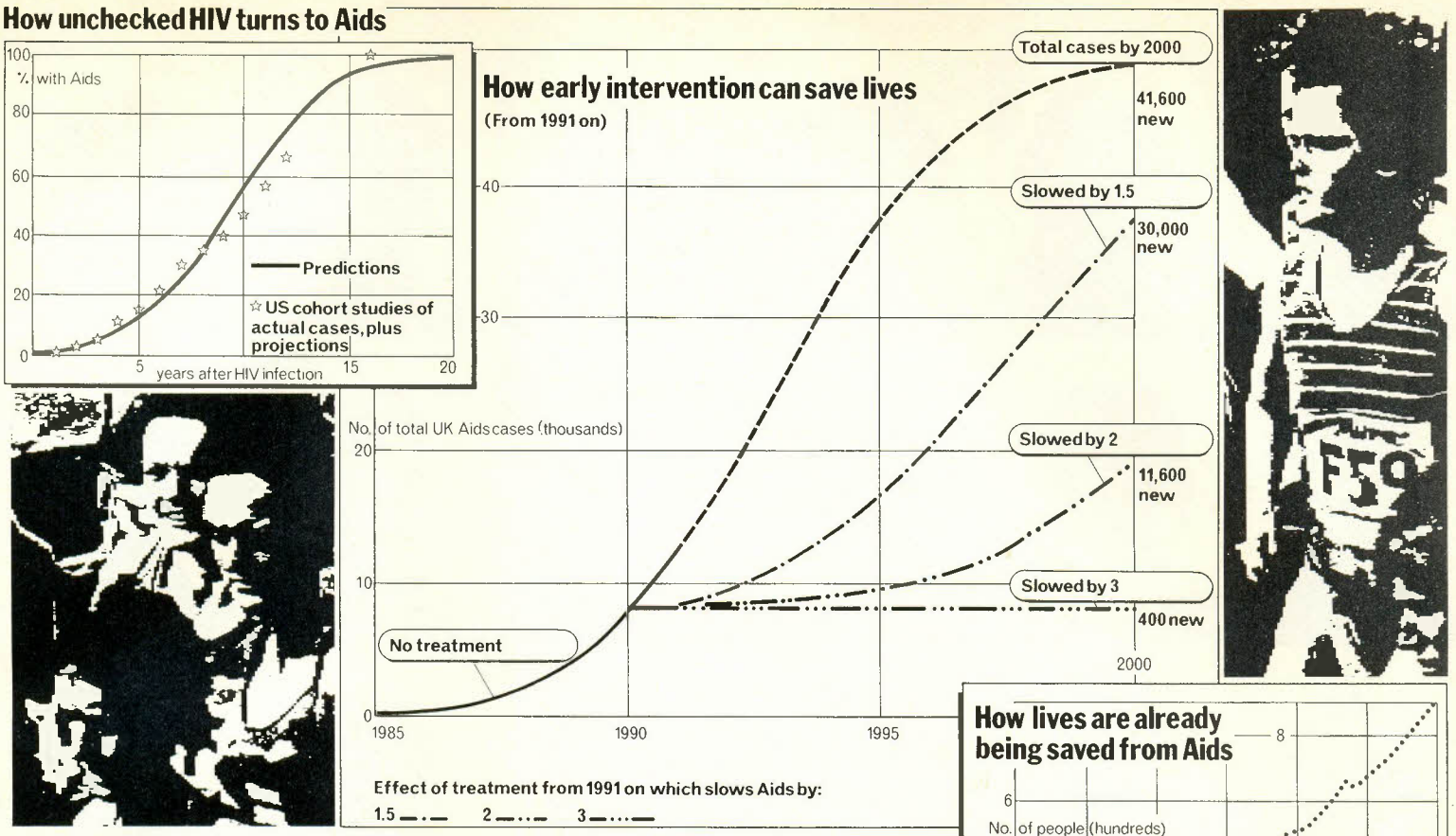
- *Vaccines* could have the same valuable effect as education in safer sex, but they are very unlikely to work—not, at least, until there is a cure for the syndrome itself.

No vaccine proposal has as yet shown any promise. Professor Arie Zuckerman of the University of London, speaking at the "Global Impact of Aids" conference in March this year, warned the assembled international experts that with vaccines there was "no cause for optimism". All eight vaccine candidates tested to date, he said, have proven unpromising. "Because of the lengthy incubation period, it is extremely unlikely that any general anti-HIV vaccine will be available for five to ten years, and probably longer." Three months later, top British researcher Dr Robin Weiss, director of the Institute for Cancer Research, told the Stockholm 4th International Aids Conference that "There's everything against (a vaccine). The very nature of the virus is self-defeating (even though) every conceivable approach is being tried."

- The tide *is* expected to turn, on vaccines as well as other research objectives. But in the meantime—*now*—it is vitally important to go down the fourth path—that of "early intervention".

Since the beginning of 1988, US doctors, clinics and self-help groups have begun this new and promising attack on Aids. The key idea is to arrest the virus's effects before they turn into "full-blown" Aids. These researchers have accepted that public hopes for a vaccine against HIV have to be abandoned for the moment, and that full-scale cures are still distant. But they recognise that early intervention methods have the potential to transform the Aids epidemic into a disease which is at least as manageable as diabetes. A leading American Aids researcher, Dr Bernard Bihari of the State University of New York, said last month that he hoped that "within 12-18 months, we'll be able to arrest the disease (HIV) at whatever stage it's at."

Not all researchers and clinicians share Bihari's optimism that medical progress could be so rapid, although almost all now think that early intervention is both feasible and essential. Their views are not a pipe dream. Even with the much more serious problem of Aids itself, (late)



GRAPH 1: HIV infection gradually turns into Aids for almost everyone infected. After 10 years, US cohort studies have found that half those infected have developed Aids, and another 25 per cent are ill (though not with Aids itself). Using these and other studies, it's possible mathematically to predict (continuous line) the grim long-term results of HIV infection.

GRAPH 2: The top line traces the results of the Cox report's estimates that a maximum 50,000 people are infected with HIV. If left untreated, 49,000 of them will have developed Aids by the year 2000. If an early intervention programme were begun by 1991, it could save most lives at risk reducing the number of new Aids cases from an expected 41,600 to 400!

GRAPH 3: Intervention is already saving the lives of people suffering from full-blown Aids. New drugs and preventive treatment have *reduced* the average annual death rate from Aids in Britain while the number of people with Aids has *risen*. In two years their chances of surviving have become up to three times better, given proper treatment.

medical intervention can be shown already dramatically to have improved both the quality of life and the survival prospects for people who have developed Aids, once regarded as an immediately terminal disease (see graph 3).

That work will continue, but the problem now, say Bihari and his colleagues, is to stop ten to one hundred times more people from developing the disease. To remedy deficiencies in US research, he and a team of leading US east coast Aids researchers, including Mathilde Krim and Joseph Sonnabend, two of America's leading Aids physicians, have pioneered the "Community Research Initiative" aimed *inter alia* at finding how to prevent HIV turning into Aids. "The goal is to stop Aids," says Sonnabend, not to treat it or cure it. If they succeed, the new "great plague" scares of the early 1980s could well be ancient history by the early 1990s.

The key to early intervention strategies lies in accepting the grim significance of "progression" studies such as Weller's. It took several years of carnage before epidemiologists could say with assurance that no "co-factor" or second cause was necessary to turn HIV infection into full-blown Aids. (If so, it could have been attacked in place of the complex and seemingly ineluctable HIV virus.) Even if other infections or poor general health *speed* progression to Aids, they do not appear to be essential *ingredients* of the disease. Once this was known for sure, the fight to erect a safety net against Aids could focus on the HIV virus alone.

Early intervention operates on the premise that the important thing is to attack or restrain HIV before it has done its work of destroying the immune system. In particular, it has to be done while there is enough immunity left to destroy or help destroy other new infections, while the patient is still sufficiently healthy to resist the toxic effects of powerful drugs. Drugs also work much better on patients whose immune systems are still relatively intact.

America's most prominent Aids scientist, Dr Robert Gallo, of the US National Cancer Institute, told the Royal College of Physicians last spring that using anti-viral drugs only *after* someone had been diagnosed with Aids was "almost certainly too late". It was now essential to use them as early as possible. If *he* got infected, Gallo said firmly, he certainly wasn't going to wait to get sick to start treatment.

At first, leading epidemiologists such as Dr Andrew Moss of the University of California guessed that an effective early intervention therapy—which could involve dietary and psychological factors as well as drugs—would have to slow HIV's destructive effects over time by a factor of at least five and perhaps ten or more. But the long-term path of HIV infection remained difficult to calculate exactly. Then, in an epochal study published by the *British Medical Journal* last March, Moss and colleagues showed for the first time how to predict reliably the long-term effects of HIV infection. Moss reported that the prognosis for the men he studied "is clearly worsening over time... We should regard progression to clinical Aids following HIV infection as the norm rather than the exception".

Using projections based on Moss's and related "cohort" studies (of groups of people infected about the same time), it can be shown that relatively minor early intervention strate-

gies will have a major effect on the long-term effect of the epidemic. If, for example, (as the Cox working party found) there may be 50,000 people presently infected in Britain, some 34,000 of these will have developed Aids by 1995. By the year 2000, all but 500, plus any who have died earlier of other causes, will have developed Aids. But if the effects of the virus were slowed by only a factor of 1.5, 15,000 fewer people would have Aids by 1995 (see figure 2). Slowed by the larger factor of two (that is, doubling the time which people take to progress to Aids), only 12,000 more people (instead of 42,000) would have developed Aids by the year 2000.

If HIV can be slowed by a factor of three, then the projected British Aids toll after 1991 falls from 42,000 or so to a mere 400. Aids would no longer be a major public health problem. So, although early intervention won't immediately eradicate Aids or the HIV virus, it can curb more than 90 per cent of the death and suffering we can expect in the short and medium terms. By targeting anti-infection advice more efficiently it will also help limit further infection. And it would generate a life-saving breathing-space while full-scale cures and vaccines are found.

"It's an excellent approach," Dr Weller said last month. "It makes good clinical sense." Weller said he was impressed by the dramatic long-term effects of early therapy. "We have to stop simply observing what's happening," he said, "and start therapeutic intervention." At the University of California, Dr Moss said he agreed that the way the effects of early intervention had been calculated were appropriate. "We can't justify prospective studies any more. We have to intervene."

The new approach is already being tried, successfully, by pioneering clinics in the United States and Europe. At the University of Amsterdam, researchers have found that the well-known anti-Aids drug, AZT or zidovudine, appears to work better and cause fewer side effects when given to people who *haven't* yet developed Aids. In San Francisco, a new clinic concentrating almost exclusively on early intervention, Positive Action Healthcare, has quickly won a high reputation and has attracted hundreds of patients since it started operations just one year ago. Its director, Dr Alan Levin, has made publicly available all of the data on their attempted therapies and the effect on patients, so that they and other physicians alike may judge which stand the best chance of success.

Thousands of people will die for every month that is lost if the new methods are not tested and implemented as soon as possible. Yet research on this, the most vital Aids-limiting task after public health education, has scarcely begun in Britain or anywhere else—despite the fact that the lives most easily saved will be the most recent potential casualties of HIV infection, particularly those affected by the new, slower growing heterosexually-transmitted epidemic.

Until a few months ago, no money was being spent on such research in Britain. The first Aids doctor in Britain who proposed a simple project along these lines was refused funds, 18 months ago. In the Medical Research Council's July 1988 report on its Aids "Directed Programme", there is not a single proposal for early therapeutic intervention to curb the morbidity of HIV infection. Although £14 million has already been committed, and a further £16 million was promised by the government to the MRC Aids "Directed Programme" two months ago, none of this money is to be available for clinical trials, even for full-blown Aids.

What makes this particularly scandalous is that such funds *are* available for vaccine trials. The concentration of research on vaccines and the theoretical study of viruses to the exclusion of urgent clinical trials with *patients*—which is as true of the United States as of Britain—has already driven American Aids activists into weekly direct action protests against the medical and government research establishments. They believe that Aids is not being researched or treated properly because it is still officially regarded privately only as a gays' or junkies' disease. John James, editor of *Aids Treatment News* in San Francisco, claims that in the United States there is an "ill concealed *de facto* public policy to write off those already ill or infected with HIV". Tony Whitehead, founder of Britain's leading Aids charity, the Terrence Higgins Trust, says that "treatment is being left to the drugs companies. If it is seen not to affect the so-called 'general public', it doesn't matter."

We have to stop simply observing what's happening and start therapeutic intervention

To its credit, the MRC pointed out to the government last June that at least £40 million more should have been allocated to Aids research over the next three years, or other important medical research would necessarily suffer. All these sums are, nevertheless, trivial in comparison to the likely losses of billions of pounds if the research is *not* done.

One trial has now been launched, to test the effectiveness of zidovudine (AZT) in early intervention, involving up to 2,000 people at 60 centres in Britain and France. The trial is based on the *minimum* hypothesis that the drug will at least halve the rate at which Aids develops, and that side effects will not outweigh efficacy.

Meanwhile, other features of the British Aids epidemic suggest that even with the less tractable problem of Aids itself, the news is good. Few people have realised that the reporting rate for new Aids cases in Britain has virtually been flat since spring 1987. Unless hospitals are getting worse rather than better at identifying and reporting Aids (which is highly unlikely), then it is clear that the period of exponential epidemic growth of Aids in Britain is already over.

The main reason why this has happened is almost certainly that long before the government launched its education campaigns, gay men in Britain had effectively changed their sexual behaviour to limit the spread of HIV—a phenomenon that has also been seen in major US cities. According to studies for the recent Cox report, this may have happened as early as 1983—two years *before* the government began to pay attention to the problem. But changes in gay sexual behaviour went unrecognised. So *all* the previous projections of Aids cases in Britain have turned out to be wrong, largely because they implicitly or explicitly adopted erroneous, wildly speculative assumptions about gay men's careless sexual abandon.

The government's Centre for Disease Surveillance and Control predicted two years ago that there would be 1,837 Aids cases by 1988. The non-governmental Office of Health Economics last year predicted about 3,000 cases. Insurance companies have been basing their plans to discriminate against single men on even wilder scenarios. No statistician predicted fewer than 1,200 cases for 1988, and all have been wrong. The actual number of Aids cases reported in Britain last year was about 700 (635 had been reported by the end of November). Cox's projections of HIV infection, although still too high for 1988, appear far more accurate.

While the rate of new cases remains flat, the number of people living with Aids in Britain is continually increasing. Yet the death rate is actually *dropping* (see figure 3). The average annual death rate, which three years ago equalled the number of people living with Aids, is now one third of that level, and heading down. With better Aids treatments, it should soon be possible to say that someone had had Aids but had recovered; such changes in perceived as well as actual medical practice have already occurred with many cancers. Once early intervention has made the decline linked to HIV arrestable, it may also be made *reversible*.

Even in the five earliest—and worst—years of the epidemic, in New York, 15 per cent of people who had had Aids for five years were still alive. One of the main organisers of New York's "People with Aids Coalition", singer Michael Callan, remains energetic, active and well, almost *seven years* after he was diagnosed. But despite the optimism now creeping in around Aids, the virus and its genes are going to be a problem for a very long time. Most people now sexually active will probably always have to make their sexual behaviour "safer"; and in the late 1990s, unless heterosexual habits change, it will be heterosexuals rather than homosexuals whose behaviour puts them at grave risk. Early intervention won't change the risks, but it will change the consequences.

In last month's government report on the short-term prediction of Aids and HIV infection, the authors made the working assumption that "there will be no medical development, vaccine or treatment that will make a major change in the determining features of the epidemic in our time frame (to 1992)". This is understandable and reasonable, since the government epidemiologists could not predict what medical advances might render their future projections inaccurate, *even though* such changes have already begun. But projecting the future course of the epidemic is only the beginning of the problem. The epidemiologists have only interpreted the world; the point is to change it. ●

Additional research by Dr Janie Grote and Nigel Townson