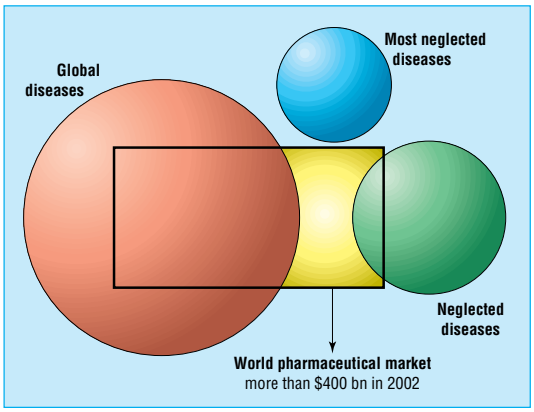

Three types of diseases

drug research and development. The patients have no purchasing power, no vocal advocacy group is pleading for their needs, and no strategic interests—military or security—are driving concern about these conditions. This is why no public-private partnerships exist specifically for the most neglected diseases. The figure shows how these diseases fall totally outside the global pharmaceutical market.

For example, sleeping sickness, which claims thousands of lives annually in Africa, can be considered as a most neglected disease. Current drug treatments are in scarce supply, difficult to administer, and often toxic. Melarsoprol, which was developed over 50 years ago, kills up to 10% of people who are given the drug, and in some regions drug resistance means it is ineffective in a third of patients.[3] An effective, less toxic drug, has been developed—eflornithine—but the company that developed it stopped its production in 1995, citing commercial failure. African patients could not afford to buy the drug. Eflornithine became available again five years later in the United States, when it was found to reduce unwanted facial hair in women.[4] The injustice of American women depilating their faces while thousands in Africa were dying of a treatable illness finally led the original makers to restart production of the drug.[5] It is currently available through a donation programme until 2006, though a long term producer is yet to be found.

Médecins sans Frontières believes that the best hope of treating the world's most neglected diseases is for the public to accept responsibility for drug development, taking it out of the marketplace and into the public sector. The organisation has launched an initiative on drugs for neglected diseases, founded only by public sector and non profit partners, such as the Pasteur Institute, the Special Programme for Research and Training in Tropical Diseases (a project undertaken jointly by the United Nations Development Plan, the World Bank, and the World Health Organization), the Indian Council for Medical Research, and the Brazilian government pharmaceutical organisation Fiocruz. The initiative is testing the idea that a drug research and development network can be established in the developing world, with a centralised management structure, and its feasibility study will be published later this year. Philippe Kourilsky, the director general of the Pasteur Institute, believes that the initiative will do "nothing short of creating a global, not-for-profit pharmaceutical industry." If the initiative proves viable, it is likely to engage with the pharmaceutical industry on specific projects, since industry has great expertise in the development of drugs. The initiative, however, will not rely on market forces; it will define its needs, and then rely on public investment to meet them.

Will the strategy of taking medicines out of the marketplace work? Few precedents for truly international public initiatives exist (the Human Genome Project is an example), and the public investment will need to be massive. There will need to be concerted political attention to make available the necessary financial and technical resources. Right now there is little other hope for those dying of the world's most neglected, yet curable, infectious diseases.

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Performance league tables

Use of indirect standardisation is inappropriate

Valid performance league tables cannot be formed from indirectly standardised indices.[1–5] However, this methodology has been adopted for most of the performance indicators for NHS trusts that relate to outcomes, effectiveness, and access. This includes all the clinical indicators.[6] Indirect standardisation is also used to compare general practitioners' prescribing.[7]

As an illustration, the example in the box includes two study populations with identical category specific rates (these may be for age, ethnicity, or case mix, for example). Despite performing identically, they have two very different indirectly standardised ratios because of their different structures.

The inappropriate comparison of performance using indirect standardisation arises because of a common misconception about the standard that is being used. For indirect standardisation the study population itself is the standard, as this is the population to which the category specific reference rates are applied. Consequently, a different standard is used for each population's indirectly standardised ratio.

In contrast, for direct standardisation each study population's category specific rates are applied to the

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same reference population. This provides a common standard through which the directly standardised rates can be compared. Identical performance produces an identical directly standardised rate.

Indirect standardisation can be used to make valid comparisons of performance in two situations.[8] One is when each study population has an identical distribution. The second is when the rates in a study population are all the same multiple of the reference population's rates. Different populations may have a different multiple. A pragmatic view is that these conditions apply approximately to most situations where indirect standardisation for age and sex is used for health related data,[4] as in the NHS performance indicators.

The following examples show that this assumption is not necessarily justified. The Department of Health publishes three year mortality figures relating to several indicators for health authorities in both direct and indirectly standardised form.[9] Ranking for deaths from circulatory diseases for the 99 health authorities differ by up to 18 ranks between the two methods of standardisation. The average difference is 3.6 ranks, and if a threshold is drawn for the worst quarter on the basis of indirectly standardised ratios then three health authorities are incorrectly placed in this quarter.

The patterns for other health authority performance indicators are similar, and the magnitude and direction of the errors in ranking may be systematic. For circulatory disease and cancer mortality the errors are significantly correlated (Pearson's correlation coefficient 0.36, $P < 0.001$). This suggests that using a basket of performance indicators may not solve the problem of using indirectly standardised indices.

The Department of Health does not publish the information to allow the assessment of the error in their league tables for NHS trusts. With these smaller populations, misclassification will occur more often because of the greater variability in the age and sex structure. The five year mortality figures for coronary heart disease for the 101 general practices in the Lincolnshire health authority area (unpublished data) show that the practices are incorrectly placed by up to 30 ranks when using indirectly standardised ratios. A fifth are misclassified by more than 10 ranks.

Direct standardisation is the simplest way to adjust for risk when comparing performance,[1] but has its own disadvantages. Rates may not be stable from year to year, with small populations and low numbers of events. This applies to many NHS performance indicators, but using three or five year figures to stabilise rates does not suit political timetables. Information to calculate rates is not always collected, as in the case of the general practitioners' prescribing indices. Also, confidence intervals for directly standardised rates are relatively wider than confidence intervals for indirectly standardised rates.[10]

League tables are here to stay. There are many issues on how risk adjustment should be incorporated into them.[11 12] The difficulties dealing with the wide overlapping confidence intervals around individual ranks are considerable, with the multiple comparisons inherent in league tables.[12] Explaining these uncertainties to a wider public to aid the interpretation of the tables is equally problematic.

The crucial requirement for league tables is that they are based on a valid comparative measure of performance. The indirectly standardised indices currently used are fundamentally flawed in this respect. Organisations censured or not rewarded as a result of their use may be able to argue that the process has been arbitrary and unfair. If direct standardisation produces a different outcome then they can prove it.

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Performance cannot be compared using indirectly standardised ratios (for example an SMR)

An example of identical performance producing very different indirectly standardised ratios in equally sized populations

Category specific rates

Category	Both study populations	Reference population
First	30	25
Second	10	15

(rates are number of events per 1000 people per year)

The reference population rates are applied to the study population categories to produce the expected number of events in the study population. The indirectly standardised ratio is calculated by dividing the number of observed events by the number of expected events. This is commonly multiplied by 100, as for an SMR

Population 1

Category	Number people	Observed events	Expected events	Indirectly standardised ratio
First	1000	30	25	
Second	9000	90	135	
Total	10 000	120	160	0.75

Population 2

Category	Number people	Observed events	Expected events	Indirectly standardised ratio
First	9000	270	225	
Second	1000	10	15	
Total	10 000	280	240	1.17

It is possible to have the lowest indirectly standardised ratio in the population with greatest rates and the largest number of events

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