BEHIND THE HEADLINES

Behind the Headlines reproduces selected clinical articles which have been published online in *The Bulletin* in the preceding quarter, in order to disseminate this topical clinical information to a wider audience (including those Fellows and Members without internet access).

The reproduced articles aim to educate and inform the wider College membership about specialist items that have been reported in the international medical and mainstream media: to the non-specialist it may not always be clear how accurately such stories – whether reporting results of scientific studies or issues of concern to health professionals – have been reported. To clarify such situations, expert clinical comments are commissioned on matters that are recurring in the international media, or about which different reports have caused conflicting messages for those practising in other specialties.

It is hoped that this section will, in time, become an invaluable source of independent and authoritative advice for Fellows and Members interested in updating their knowledge of new developments in other specialties.

IN THIS ISSUE

- Antiretroviral therapy in adolescents and adults in resource-constrained countries;
- Prehypertension and high normal blood pressure – a paradigm shift in the management of cardiovascular risk?; and
- Lung-volume-reduction surgery for emphysema: the National Emphysema Treatment Trial (NETT).

ANTIRETROVIRAL THERAPY IN ADOLESCENTS AND ADULTS IN RESOURCE-CONSTRAINED COUNTRIES

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BACKGROUND

During the last year there has been a considerable amount of international media coverage devoted to the worldwide increase in HIV/AIDS and to the problems faced by developing countries when seeking to treat this disease. Against this background it was decided to commission this comment from Professor Taimor Nawaz, Professor of Medicine, Bangladesh Medical College, who was responsible for developing the World Health Organization (WHO) South East Asia Regional Office (SEARO) guidelines, *The use of antiretroviral therapy: a simplified approach for resource-constrained countries*, in 2002.

At the end of 2002, an estimated 42 million people globally were living with human immunodeficiency virus (HIV). In the same year, there were an estimated five million new infections, and a loss of more than three million lives related to the acquired immunodeficiency syndrome (AIDS) epidemic.[1] Most of the new infections occur in developing countries. Current projections suggest that an additional 45 million people will become infected with HIV in 126 low and middle-income countries between 2002 and 2010. Expansion on a global scale of successes of prevention programme of some countries by 2005 may prevent 29 million new infections by 2010.[1, 2] Clearly, preventive strategies require greater support.

Millions of people infected with HIV in developing countries face disease and early death unless they receive appropriate medical care. The World Health Organization (WHO) estimated that in 2002 some six million in developing countries were in need of antiretroviral treatment. Instead, only 230,000 had access to them, and half of these lived in Brazil. The United Nations General Assembly Special Session on HIV/AIDS (UNGASS) in 2001 expressed the need for combining HIV infection prevention and care including the use of antiretroviral treatment.[3]

Problems related to the use of antiretroviral drugs in developing countries have been medium/long-term availability and affordability of drugs and the lack of health infrastructure necessary to use them. Furthermore, there are concerns that difficulties with adherence to complicated medication regimens would promote drug resistance.[4, 5] However, the use of highly active antiretroviral therapy (HAART) as a part of comprehensive care in the poorest countries is now an urgent priority and should complement programmes to prevent HIV transmission. Antiretroviral therapy (ART) has transformed the disease into a treatable and chronic condition.[6, 7] The reasons for combining HIV infection prevention and therapy include a humanitarian rationale, to save children and the fabric of the society, for continuing economic development and to optimise preventive efforts. When testing is linked to therapy, people have an incentive to be tested, providing a rational response: primary prevention for HIV-negative persons and therapy

for HIV-positive patients.[8] Pharmaceutical companies in some of the developing countries are now manufacturing generic drugs at a much lower cost compared to developed countries making it possible for these drugs to be made available for resource-limited settings. The Global Fund to Fight AIDS, Tuberculosis and Malaria was launched in 2001 and is a significant new financial investment to combat these diseases in developing countries.

Specific services and facilities are most desirable before starting ART due to the complexity of the therapy, the need for monitoring and the cost of therapy.

These services include:
1. Access to HIV voluntary counselling and testing (VCT) and institution of follow-up counselling services to ensure continued psychosocial support and to enhance adherence to treatment.
2. Medical services capable of identifying and treating common HIV-related illnesses and opportunistic infections.
3. Reliable laboratory services capable of doing routine laboratory investigations such as complete blood count and chemistry. Access to referral laboratory capable of doing CD4+T lymphocyte count is desirable to monitor therapy.
4. Reliable and affordable access to quality antiretroviral drugs, and drugs to treat opportunistic infections and other related illness.

CLINICAL EVALUATION

Before starting therapy, patients should have the following performed:
- complete history and physical examination; and
- laboratory investigations.

A detailed clinical evaluation is essential prior to initiating antiretroviral therapy and should aim to:
- assess the clinical stage of HIV infection;
- identify past HIV-related illnesses;
- identify current HIV-related illnesses that will require treatment; and
- identify co-existing medical conditions and treatments that may influence the choice of therapy.

HISTORY AND PHYSICAL EXAMINATION

A medical history should include the following questions:
- when and where was the diagnosis of HIV made;
- what is this person's possible source of HIV infection;
- what are the current symptoms and concerns of the patient;
- past medical history of symptoms, known diagnoses and treatment given;
- history of symptoms of or previous treatment for tuberculosis;
- history of possible contact with tuberculosis;
- history of possible sexually transmitted infections;
- history of pregnancy in a woman;
- history of previous antiretroviral therapy;
- history of medication and oral contraceptive use in women; and
- social habits and sexual history.

The physical examination should include the following points:
- patient's weight;
- skin: herpes zoster, Kaposi's sarcoma, HIV dermatitis;
- lymphadenopathy;
- oropharyngeal mucosa: candidiasis, Kaposi's sarcoma, hairy leucoplakia;
- examination of heart and lungs;
- examination of abdomen particularly for liver and spleen enlargement;
- examination of neurological and musculoskeletal system: mental state, motor and sensory deficit;
- examination of optic fundus: retinitis and papilloedema; and
- examination of the genital tract/gynaecological examination.

LABORATORY INVESTIGATIONS

Essential:
- HIV serology;
- CD4+T lymphocyte count or total lymphocyte count (TLC);

- complete blood count and chemistry (serum ALT or AST, serum creatinine and/or blood urea nitrogen, and plasma glucose); and
- pregnancy test.

Supplementary tests indicated by history and physical examination:
- chest X-ray;
- urine for routine and microscopic examination; and
- hepatitis C virus (HCV) and hepatitis B virus (HBV) serology.

Other tests which may be indicated include serum lipids, serum bilirubin and serum amylase.

Although HIV viral load (plasma HIV RNA level) is a strong predictor of clinical outcome,[9] in resource-limited settings, an assessment of viral load is not considered essential to start therapy.

INDICATIONS

Table 1 sets out recommendations for initiating ART in adults and adolescents.

TABLE 1
Recommendations for initiating antiretroviral therapy in adults and adolescents* with documented HIV infection.[10, 11]

If CD4 testing is available:
- WHO Stage IV disease irrespective of CD4 cell count†
- WHO Stage I, II or III† with CD4 cell counts <200/mm³‡

If CD4 testing is unavailable:
- WHO Stage IV disease irrespective of total lymphocyte count
- WHO Stage II or III disease with a total lymphocyte count <1,200/mm³§

* Adolescents >13 years of age should receive ART based on adult guidelines according to body weight.

† Treatment is also recommended for patients with advanced WHO Stage III disease including recurrent or persistent oral thrush and recurrent invasive bacterial infections irrespective of CD4 cell or total lymphocyte count.

‡ The precise CD4 count above 200/mm³ at which to start ART has not been established but the presence of symptoms and the rate of CD4 cell decline (if measurement is available) should be factored into the decision making CD4 count of 200/mm³ corresponds to a CD4 percentage of approximately 15%.

§ A total lymphocyte count of <1,200/mm³ can be substituted for the CD4 count when the latter is unavailable and HIV-related symptoms exist. It is less useful in the asymptomatic patient. Thus, in the absence of CD4 cell testing, asymptomatic HIV-infected patients (WHO Stage I) should not be treated because there is currently no other reliable marker available in severely resource-constrained settings.

For WHO Stages I–IV, please refer to the Appendix.

ANTIRETROVIRAL DRUGS

Table 2 outlines the 12 antiretroviral drugs included in the WHO Model List of Essential Medicines in April 2003.[12, 13]

TABLE 2
Antiretroviral drugs.

Nucleoside reserve transcriptase inhibitors (NsRTI)
- (NNRTI)
- abacavir (ABC)
- didanosine (ddI)
- lamivudine (3TC)
- stavudine (d4T)
- zidovudine (ZDV or AZT)
- Protease inhibitors (PI)
- indinavir (IDV)
- ritonavir (RTV, R)*
- nelfinavir (NFV)
- saquinavir (SQV)

Non-nucleoside reverse transcriptase inhibitors
- efavirenz (EFV or EFZ)
- nevirapine (NVP)

*Ritonavir is recommended for use in combination with indinavir, lopinavir and saquinavir as a booster and not as a drug in its own right.

CHOICE OF REGIMEN

For antiretroviral therapy in special situations (pregnancy, tuberculosis, opportunistic infections and hepatitis), the reader is referred to published guidelines.[10, 11]

MONITORING THERAPY

Table 3 provides recommended ART regimens for adults and adolescents.

TABLE 3
Recommended first-line antiretroviral regimens in adults and adolescents.[10, 11, 14, 15]

Regimen*	Recommendation
ZDV/3TC plus EFZ or NVP	Recommended
ZDV/3TC/ABC	Consider for patients with low viral loads (if possible to determine) and adherence concerns
ZDV/3TC plus RTV-enhanced PI (IDV/r, LPV/r, SQV/r) or ZDV/3TC/NFV	Consider

*ZDV/3TC is listed as initial recommendation for dual NsRTI component based on efficacy, toxicity, clinical experience and availability of fixed dose formulation. Other dual NsRTI components can be substituted including d4T/3TC, ZDV/ddI and d4T/ddI depending upon country-specific preferences. ZDV/d4T should never be used together because of proven antagonism. Fixed dose formulations are preferred whenever possible as they promote enhanced drug adherence. Efavirenz is contraindicated in pregnancy.

After starting ART, the patient should be seen at one month and subsequently for follow-up every three to four months. Adherence should be assessed and routinely reinforced. A high degree of adherence to antiretroviral drugs is necessary for optimal virological suppression.[16]

In resource-limited settings monitoring of disease progression and response to treatment will be by clinical indicators and CD4 cell count. Patients should also be monitored for adverse drug reactions.

It may not be possible to perform viral load due to the cost of the test and the lack of laboratory facilities and trained personnel.[17] Despite concerns about the viral resistance, drug-resistance testing is not possible in most developing countries.

Some of the clinical indicators of response to therapy are:[18]

- gain in body weight; and
- decrease in frequency and severity of opportunistic infections.

Karnofsky score may be used to assess the clinical/performance status of the patient.[11]

Complete blood count and chemistry (serum ALT or AST, serum creatinine and/or blood urea nitrogen, and plasma glucose) may be repeated every three to four months and CD4 cell count may be performed every three to six months. In patients on optimal ART, CD4 cell counts usually increase by >100 cells/mm^3 in the first six to 12 months in antiretroviral naïve adherent patients with drug-susceptible virus. However, this response may be variable.

PROGRAMME IMPLEMENTATION

Before implementing an antiretroviral therapy programme in a resource-constrained country, it is essential to assess the situation to estimate the burden of the public health problem. Programme planning with clear objectives should be defined to include long-term sustainability. Adequate measures for implementation need to be taken at the programme level and health facility level to make an antiretroviral therapy programme a success.[11]

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APPENDIX
WHO staging system for HIV infection and disease in adults and adolescents

Clinical Stage I
1. Asymptomatic
2. Persistent generalised lymphadenopathy (PGL).

Performance scale 1: asymptomatic, normal activity.

Clinical Stage II
3. Weight loss <10% of body weight.
4. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis).
5. Herpes zoster, within the last five years.
6. Recurrent upper respiratory tract infections (i.e. bacterial sinusitis).

And/or performance scale 2: symptomatic, normal activity.

Clinical Stage III
7. Weight loss >10% of body weight.
8. Unexplained chronic diarrhoea >one month.
9. Unexplained prolonged fever (intermittent or constant), >one month.
10. Oral candidiasis (thrush).
11. Oral hairy leukoplakia.
12. Pulmonary tuberculosis within the past year.
13. Severe bacterial infections (i.e. pneumonia, pyomyositis).

And/or performance scale 3: bed-ridden, <50% of the day during the last month.

Clinical Stage IV
14. HIV wasting syndrome, as defined by Centers for Disease Control and Prevention (CDC).[a]
15. Pneumocystis carinii pneumonia.

16. Toxoplasmosis of the brain.
17. Cryptosporidiosis with diarrhoea >one month.
18. Cryptococcosis, extrapulmonary.
19. Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes.
20. Herpes simplex virus (HSV) infection, mucocutaneous >one month, or visceral any duration.
21. Progressive multifocal leukoencephalopathy (PML).
22. Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis).
23. Candidiasis of the oesophagus, trachea, bronchi or lungs.
24. Atypical mycobacteriosis, disseminated.
25. Non-typhoid Salmonella septicaemia.
26. Extrapulmonary tuberculosis.
27. Lymphoma.
28. Kaposi's sarcoma (KS).
29. HIV encephalopathy, as defined by CDC.[b]

And/or performance scale 4: bed-ridden, >50% of the day during the last month.
Note: both definitive and presumptive diagnoses are acceptable.

Appendix references

a HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>one month), or chronic weakness and unexplained prolonged fever (>one month).

b HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings.

PREHYPERTENSION AND HIGH NORMAL BLOOD PRESSURE – A PARADIGM SHIFT IN THE MANAGEMENT OF CARDIOVASCULAR RISK?

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BACKGROUND

This comment was commissioned following the publication, and subsequent media reporting, of new guidelines developed by the US National Heart, Lung and Blood Institute which recommended that blood pressure as low as 120/80 mmHg should no longer be classed as normal and safe, but should instead fall into the category of prehypertension.

Hypertension is a leading cause of the global disease burden, behind only malnutrition and unsafe sex. Although relatively more important in developed regions, it is also a major and growing cause of disease in the developing world.[1]

Two major guidelines for the assessment and treatment of hypertension have been published this year, from the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure in the USA (JNC 7),[2] and the European Societies of Hypertension and Cardiology.[3] While the recommendations in the two guidelines are similar in many respects, there are some differences. For example, the European guideline, but not JNC 7, emphasises the importance of overall cardiovascular risk assessment, rather than a strict focus on hypertension, when making treatment decisions.

The two guidelines classify blood pressure (BP) differently (Table 1). Perhaps the most controversial aspect of JNC 7 is that BP in the range 120–139/80–9 mmHg should be diagnosed as 'prehypertension'. No longer will doctors be able to consider a BP of 120/80 mmHg either normal or completely safe! This is largely based on data from the Framingham Heart Study showing that, within four years, hypertension will develop in 39% of 35–64 year olds and 53% of 65–94 year olds if baseline BP is 130–9/85–9 mmHg, and 18% of 35–64 year olds and 29% of 65–94 year olds if baseline BP is 120–9/80–4 mmHg.[4] The European guideline does not use the term prehypertension. It does, however, identify BP in the range 130–9/85–9 mmHg as 'high normal' BP. It then recommends that people with high normal BP initiate lifestyle measures, have other risk factors corrected and, if cardiovascular risk is high, start antihypertensive treatment. This approach is consistent with that recommended in JNC 7, indicating that this

TABLE 1
Classification of BP levels (mmHg) in the European and JNC 7 guidelines.

European guideline			JNC 7		
Category	**Systolic**	**Diastolic**	**Category**	**Systolic**	**Diastolic**
Optimal	<120	<80	Normal	<120	<80
Normal	120–9	81–4	Prehypertension	120–39	80–9
High normal	130–9	85–9			
Grade 1 HT (mild)	140–59	90–9	Stage 1 HT	140–59	90–9
Grade 2 HT (moderate)	160–79	100–9	Stage 2 HT	160	100
Grade 3 HT (severe)	180	110			

HT=hypertension

difference relates more to style than substance.

The European guideline categorises BP in the range 120–9/80–4 mmHg as normal, though not optimal. Therefore, it is really within these values that the approach to BP classification differs across the Atlantic. The JNC 7 report, but not the European guideline, recommends that at this level of BP lifestyle measures should be instituted and treatment initiated for compelling indications, including high coronary risk.

Will targeting prehypertension or high normal BP reduce cardiovascular disease? Lifestyle measures can reduce BP in patients with hypertension.[2,3] Although reducing BP in this way might be expected to improve clinical outcome, direct evidence that lifestyle changes, even when they are adopted, ultimately reduce cardiovascular events or mortality is currently lacking. Also, there is no evidence that lifestyle measures prevent or delay hypertension in those with higher than optimal BP, let alone whether this approach will ultimately reduce the incidence of vascular disease. However, it is unlikely that direct evidence to support the guidance on prehypertension/high normal BP will be forthcoming. Some insight may be gained from observational data, but it would be impractical – and possibly unethical – to randomise people to lifestyle measures or no lifestyle measures prospectively. Furthermore, the benefits of targeting high normal BP or prehypertension would be expected to accrue over many years, possibly decades, a much longer time period than can be examined in clinical trials.

If the recommendations of the European guideline are adopted then full assessment of cardiovascular risk will be required in all patients with high normal BP. This would require formal diagnosis, after at least three separate BP measurements, an ECG, and measurement of abdominal circumference and plasma creatinine, lipids, glucose and, using a high-sensitivity assay, C-reactive protein (a new development). Lifestyle advice would then routinely be required, and some patients might need drug treatment. This is all likely to considerably increase clinical workload. In the US, 13% of the adult population have high normal BP.[5] The burden of hypertension is greater in Europe than in the US.[6] Therefore, while the increased workload might be greater here in Europe, we should probably take on board the prehypertension message even more seriously.

Will this approach to the prevention of cardiovascular disease be cost-effective? Cost-effectiveness will be difficult to measure, especially given that the benefits themselves are difficult to quantify. Nevertheless, in a resource-constrained healthcare system it is likely that widespread implementation will be at the expense of other, perhaps more cost-effective, healthcare measures.

Current practice in cardiovascular risk management is to target intervention at those at high risk of an event within ten years. Most people with high normal BP or prehypertension have a low ten-year risk. However, ten years is often not a relevant time frame for these people, especially when they are young. More relevant, is that they are at high risk relative to others of similar age. For some years the entire population has been encouraged to adopt a healthy lifestyle. In an attempt to combat cardiovascular disease in its early stages it seems rational that we should target this advice to people with high relative risk, even if this is a large group. Currently, however, we do not adequately manage patients at high risk. For example, in England, 46% of hypertensives were aware that they had hypertension. Of these, just over half were on treatment and, of those on treatment, just under a third were controlled to recommended values. Overall, just 9% of hypertensives had their BP controlled.[7] Some would maintain that targeting intervention to those at high absolute risk should remain the priority.

The terms prehypertension and high normal BP are not supposed to suggest the presence of disease, at least not

yet. Those with prehypertension, however, are referred to as patients in JNC 7. What will patients think of these BP categories? Many people previously considered entirely normal will now be labelled with a medical condition. Both guidelines appear to have been produced without wider consultation of the general public. Given the potential for widespread medicalisation this seems rather paternalistic. For example, public opinion might have been useful in deciding on terminology. Prehypertension has a more definitive ring to it; the patient is left with little doubt that they are no longer medically normal. This might have advantages. Perhaps it is more honest? Perhaps it will be more likely to provide the impetus for lifestyle change? Nevertheless, such an approach runs the risk of having a negative influence on perceptions of health in the population.

The identification and management of high normal BP has the potential to substantially improve the cardiovascular health of the nation. The principle, however, must first be accepted by the medical community, which will then have to take on the considerable challenge of implementation in clinical practice.

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LUNG-VOLUME-REDUCTION SURGERY FOR EMPHYSEMA: THE NATIONAL EMPHYSEMA TREATMENT TRIAL (NETT)

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BACKGROUND

This comment was commissioned following the early online publication of the results of the National Emphysema Treatment Trial (NETT) in the *New England Journal of Medicine* and subsequent international media coverage of this significant surgical development.

Lung-volume-reduction surgery (LVRS) has been proposed as a palliative treatment for patients with severe emphysema. The procedure leads to a decrease in lung volumes and an increase in elastic recoil of the lungs. Decreasing lung volumes improves respiratory muscle geometry and hence performance, while increasing elastic recoil increases expiratory airflow, leading to improved exercise performance and reduced dyspnoea. However uncertainty over the preoperative predictors of benefit and the effects on morbidity and mortality led to a National Institutes of Health-sponsored multicentre randomised control trial in the US, comparing LVRS with medical therapy for patients with severe emphysema. The outcome of this trial has recently been published in the *New England Journal of Medicine*.[1,2]

Before randomisation, all of the patients in this trial underwent pulmonary rehabilitation. The primary outcome measurements were overall mortality and maximum exercise capacity two years after randomisation with secondary outcomes including results of six-minute walking test, lung-function tests and general health-related quality of life.

In the trial, 1,218 patients with severe emphysema, as shown on CT scan assessment, were randomised to either LVRS or medical therapy. An interim analysis of the study showed that patients with the most severe disease (FEV1 ≤20/% predicted and either homogeneous emphysema on HRCT or a carbon monoxide diffusing capacity of ≤20% predicted) had a higher risk of death following surgery than medical treatment.[3] In the subsequent analysis, 140 such patients were excluded leaving 538 patients randomly assigned to surgery and 540 assigned to medical therapy.

Those assigned to surgery were more likely to have improvements in exercise capacity and quality of life but with no reduction in mortality during an average 29 months of follow-up.

However, secondary analyses showed that the effects of surgery on mortality varied widely depending on the presence of predominantly upper-lobe emphysema on high-resolution computed tomography of the chest and whether the patient had a high or low exercise capacity at baseline after pulmonary rehabilitation defined as a maximum work load at or below a cut-off value of 25 watts for women and 40 watts for men. In patients with predominantly upper-lobe emphysema and a low exercise capacity, the risk ratio for death in the surgery compared with the medical group was 0·47 (p=0·005), indicating a significant benefit of surgery. Those patients with predominantly upper-lobe emphysema and high exercise capacity showed no benefit of surgery over medical treatment, and in those with non-upper-lobe emphysema and high exercise capacity, the risk of death was higher among those who underwent surgery.

Mortality following LRVS varies greatly among centres. The NETT research group showed a 90-day surgical mortality of 7·9% in all randomised patients compared to 1·3% in a comparably medically treated arm.[1] The majority of this mortality was accounted for by high-risk patients in whom the 90-day surgical mortality was 28·6% compared with 0% in the respective medical arm.[1] In non high-risk patients, 90-day surgical mortality was 5·2% compared with 1·5% in medically treated patients.[1] During the first year of follow-up, the mean number of in-patient hospital days per person was significantly higher in the surgical group (24·9 days) compared with the medically treated group (4·9 days p<0·001). In contrast, in the second year of the mean number of hospital days per person was significantly lower in the surgical group (3·2 days) than in the medically treated group (6·1 days, p<0·005) and in the third year there were no significant differences between the two groups in terms of the use of resources.

An economic evaluation revealed that the total medical costs were substantially higher in patients in the surgical group than for patients in the medical therapy group largely due to the costs of surgery during the course of the first six months, but from months 7–36 the mean medical cost was lower in the surgical group ($36,199) than in the medical group ($49,628, p<0·001), largely because patients in the surgical group had fewer hospital-admitted days during that period.

When the patients with high-risk conditions were excluded, the cost-effectiveness ratio for LVRS compared with medical therapy was $190,000 per quality-adjusted life-year gained. This compares, for example, with a $90,000 per quality-adjusted life-year gained for lung transplantation.[4]

The results of this trial have raised some questions about the interpretation of secondary analysis of the data collected in clinical trials. It was the purpose of the NETT trial to identify sub-groups of patients who might benefit, or be at increased risk, from LVRS. Although there appears to be an interaction between upper-lobe disease and low exercise capacity in terms of reduced mortality, there is a risk when multiple characteristics of patients are considered that there is an increased probability that one or more tests will be statistically significant by chance.

Few studies have reported long-term results of LVRS, but they suggest widely varying long-term morbidity and mortality among centres, a return of spirometric function towards pre-operative baseline and worsening of dyspnoea over time.[5]

How then are we to interpret these results and translate them to clinical practice? It appears that the findings of the NETT study provide evidence that surgery has some benefit in terms of increased exercise tolerance and survival in patients with upper-lobe predominance of emphysema and low exercise capacity compared to medical treatment. The procedure is costly, but may be cost-effective if the benefits can be maintained over time.

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