The management of pulmonary tuberculosis in the Border sub-region, 1983

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Summary

In order to study the management of pulmonary tuberculosis among black and coloured adults in the Border region of South Africa in 1983, a historical inception cohort representative of tuberculosis hospitals and local authority health services was followed up over 15 months to assess how efficiently the national responsibility is discharged in a region. About 75% of patients were sputum-positive, and 81% were judged to have had active pulmonary tuberculosis. The mean service delay after radiography was about 1½ weeks. About 26% of patients were treated with a rifampicin regimen, 50% were frequent attenders and 41% completed treatment, although about 21% were still being treated after 15 months. There was a deficiency of laboratory information for diagnosis and monitoring of response to treatment. Periodic cohort evaluation and improvement of diagnostic efficiency, of peripheral use of laboratories, and of spending on community service infrastructure are essential for closing the gap between policies and implementation.

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The diagnosis of pulmonary tuberculosis is not as straightforward as might be expected; and this is why there are difficulties in delegating management to primary care services.[1-3] It is not easy, especially in rural areas, to assemble at one place and time the clinical, bacteriological, and radiological evidence, let alone the expertise, upon which sound diagnosis is based. One of the aims of this study was to evaluate the outcome of the diagnostic process as it had to be practised in the Border region of the eastern Cape in 1983.

In programme evaluation inception cohort design is necessary to establish true proportional outcomes, and routine cross-sectional health service data are unsuitable for this purpose.[4,5] Inception cohorts should be representative of all the people for whom the service is responsible. The fragmentation of such a responsibility complicates the assembly of cohorts. The study also dealt with this problem.

Nine studies of actual service programmes have, to our knowledge, been published in South Africa since 1980.[6-14] Four reported on diagnostic status.[9,10,13,14] In 3 studies patients were reported as confirmed[8,12] or notified[7] cases of pulmonary tuberculosis; and in 2 studies this status was not discussed.[6,11] Six of these reports studied cohorts,[6,7,9,10,12,14] and 3 sought results representative of one authority or region.[7,10,14]

Particular objectives of this study were to discover for the study area: (*i*) the age-specific incidence of patients treated for pulmonary tuberculosis; (*ii*) the proportion of patients who had active pulmonary tuberculosis and who had previously been treated for the disease; (*iii*) the amount of clinical information appearing in clinical records; (*iv*) the delay after presentation before starting treatment (health service delay); (*v*) the drug regimens used initially; (*vi*) what proportions of patients were denotified, transferred out of the study area, stopped attending for treatment, and completed treatment; (*vii*) the pattern of patients' compliance with treatment; (*viii*) the pattern of sputum-conversion during treatment; and (*ix*) to compare the compliance of initially hospitalised with initially ambulant patients.

Populations and methods

The study area was the Border corridor between Ciskei and Transkei, comprising the magisterial districts of East London, King William's Town, Komga, and Stutterheim (Fig. 1).

Fig. 1. The Border study area.

The study population comprised black and coloured people aged ⩾ 15 years whose treatment for pulmonary tuberculosis in the study area had been started before July 1983.

Data from the Department of Health and Welfare (Eastern Cape) showed that about 90% of treatment in the area was provided by four health services: the South African National Tuberculosis Association hospital at Fort Grey (SANTA), the Infectious Diseases Hospital, East London (IDH), the East London City Health Department (CITY) and the Divisional

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Council of Kafraria (KDC). Sampling excluded the municipalities of Stutterheim, King William's Town, Beacon Bay, and Gonubie because they treated extremely few black patients. The four general hospitals in the area were also excluded because, although their passive case-finding role is very important, the number of cases they continue to treat is very small.

Inception cohort

A historical inception cohort was assembled by taking subsets of patients IDH + SANTA, CITY, and KDC. The names of all eligible patients starting treatment in a certain number of complete months immediately preceding July 1983 (15 months before data collection began) were taken from the treatment registers of the 12 local authority clinics and the admission registers of the 2 hospitals. The calculation of a 12-month denominator for the study area statistics is shown in Table I. The numerator for each statistic for the study area as a whole is the sum of the subset statistics each re-weighted according to the formula:

$$\frac{\text{Subset statistic}}{\text{Period of recruitment (mo.)}} \times 12$$

Data collection

A questionnaire for abstracting the required data from records was developed and pre-tested. All questionnaires were completed by one of us (R.F.I.).

Radiographic review

The initial radiographs of patients who were thought to be sputum-negative or had no sputum information available at the time treatment began, together with inactive controls, were re-read without any clinical information by 4 experienced radiographic readers who were asked to express, as a percentage probability, whether appearances were due to active pulmonary tuberculosis.[15]

Calculation of compliance

The frequency of *expected* attendance for treatment varied widely in the study area. Treatment in hospital was supervised daily; treatment in the city was supervised 5 days a week; treatment in the rural areas was given out monthly or bi-monthly. Compliance is here defined as the attendances (for either treatment or collection of treatment) expressed as a percentage of attendances expected. It was assumed that compliance in hospital and for supervised treatment at work was 100%. Calculations of overall compliance provided for changes of regimen as follows:

$$\text{Overall compliance} = \frac{(C_1 \times P_1)}{T} + \frac{(C_2 \times P_2)}{T} + \text{etc.}$$

Where C_1, C_2, etc. = percentage compliance with first, second and subsequent regimens; P_1, P_2, etc. = duration of first, second and subsequent regimens; and T = total period of treatment.

Patients were divided into the four categories of compliance used by Saunders *et al*:[7] (*i*) early drop-outs — patients who stopped receiving treatment within three months of starting; (*ii*) late drop-outs — patients who stopped receiving treatment between 3 months and 9 months of starting; (*iii*) infrequent attenders — patients who attended for > 9 months but received $< 80\%$ of expected treatment; and (*iv*) frequent attenders — patients who attended for > 9 months and received $> 80\%$ of expected treatment.

Because no uniform period of treatment pertained in the study area the last two categories were divided into those whose treatment was completed (i.e. as a result of a medical decision), those who stopped attending after between 10 months and 15 months, and those still attending after 15 months.

Incidence of active disease

To estimate the incidence of active disease being treated, patients who were transferred out of the study area were excluded on the assumption that they belonged outside the study area. Patients who were denotified were also excluded. The subset numerator was then reduced by the proportion judged to have had inactive disease, and then increased by a factor of 1,1 for the proportion of patients treated in the study area who were not sampled. The population figures for the study area in 1983 were provided by the Epidemiology Directorate: Department of National Health and Population Development (personal communication).

Confidence limits

Ninety-five per cent confidence limits will appear in brackets. The confidence intervals of proportions arrived at using weighting factors have been calculated using the formula:

$$V_W = \frac{W_1}{W}^2 \times \frac{P_1(1-P_1)}{N_1} + \frac{W_2}{W}^2 \times \frac{P_2(1-P_2)}{N_2} + \text{etc.}$$

where P_1, P_2, etc. = proportion for first, second, etc. subsets; W_1, W_2, etc. = weighting factor applied to first, second, etc. subset proportions; W = sum of weighting factors; and V_w = variance of weighted proportion.

TABLE I. APPLICATION OF WEIGHTING FACTORS TO THE COHORT SUBSETS TO PRODUCE A DENOMINATOR FOR THE STUDY AREA

Kind of service	No. of patients in subset	Recruitment period*	Weighting factor	Calculated annual No. of patients
INH + SANTA	**120**	**2 months**	**× 6**	**720 (61,7%)**
CITY	**112**	**4 months**	**× 3**	**336 (28,8%)**
KDC	**83**	**9 months**	**× 4/3**	**111 (9,5%)**
Border study area total				**1167 (100%)**

* Months preceding July 1983

Results

Completeness of data

The clinical records of 4 of the 315 patients (1,3%) studied were not available but some information was available from admission and treatment registers. Data were missing concerning compliance for 20 patients (6%) and concerning management outcome for 6 patients (2%).

Age-specific incidence of patients who began treatment (Fig. 2)

The median age (and inter-quartile range) of patients was 38 years (13 years). Most patients (24%) were in the age group 25 - 34 years; however, the peak age-specific incidence of 1 749 patients/10^5 study population shifted to the 55 - 64-year age group.

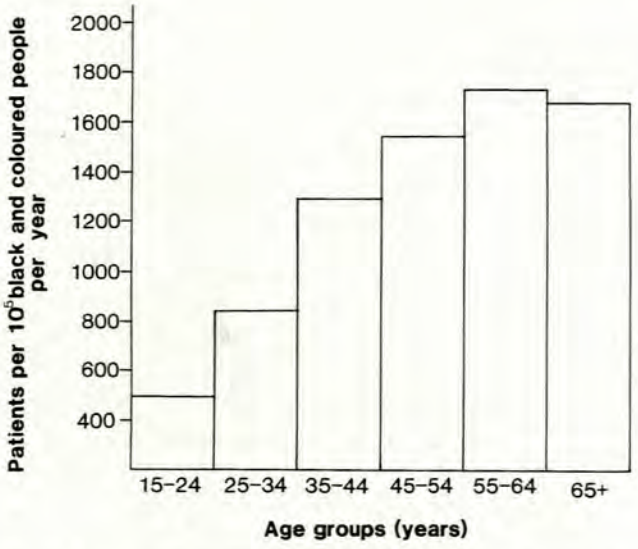

Fig. 2. Age-specific incidence of patients who began treatment.

Past history

A past history of treatment for pulmonary tuberculosis was recorded in 37% of patients (31 - 43%). A negative history was recorded in 15%. No positive or negative history was recorded in 48%. Of patients treated before, 47% had been treated within the previous 2½ years and one-third had been treated twice before.

Clinical information

A positive source of infection for new disease was identified or specifically excluded in about 8% of records. Physical signs were seldom recorded. There was no information, either positive or negative, about cough in 21%, sputum in 97%, duration of cough in 89%, or duration of illness in 45%.

Sputum status and active disease (Table II)

At the time treatment began 71% patients (66 - 76%) had been shown to be sputum-positive and 21% sputum-negative. No information was available in 8%. Of the latter two groups 20% were judged on radiographic review to have a more than 60% probability of active disease (mean of 4 readers), which is 6% of all patients. After treatment began 4% more were shown to be sputum-positive. The contrasting figures for the three services are shown in Table II. It can be concluded that altogether about 81% had active pulmonary tuberculosis (IDH + SANTA 89%, CITY 71%, KDC 59%).

Incidence of active pulmonary tuberculosis

The incidence of active pulmonary tuberculosis being treated among this population of 105 094 black and coloured people > 15 years of age in the study area in 1983 was calculated to be 745/10^5.

Delay in treatment (Table III)

The median interval between the first recorded encounter with the patient and the start of treatment was 1½ weeks. By 3 weeks 20% of patients had not begun treatment, and by 5 weeks 10% of patients had not begun treatment.

TABLE III. INTERVALS BETWEEN FIRST RECORDED ENCOUNTER WITH PATIENT AND START OF TREATMENT (WKS)

Kind of service	Median value	20% patients had not started treatment	10% patients had not started treatment
IDH + SANTA	**1**	**2**	**3**
CITY	**2**	**4**	**7**
KDC	**4**	**8**	**10**
Total for Border region	**1½**	**3**	**5**

TABLE II. SPUTUM STATUS (%) OF PATIENTS WHEN TREATMENT BEGAN OR WITHIN 2 WEEKS AFTERWARDS AND RETROSPECTIVE ESTIMATE OF PATIENTS WITH ACTIVE PULMONARY TUBERCULOSIS

Kind of service	a Sputum–positive*	b Sputum–negative*	c No sputum information	d Late sputum–positive†	e Not sputum–positive but judged active on radiographic review	Active pulmonary tuberculosis
IDH + SANTA	**82**	**16**	**3**	**5**	**2**	**89**
CITY	**63**	**26**	**10**	**1**	**7**	**71**
KDC	**26**	**39**	**35**	**5**	**28**	**59**
Border	**71**	**21**	**8**	**4**	**6**	**81**

* By direct examination.
† Direct- or culture-positive for the first time more than 2 weeks after treatment began.

Drug regimens used (Table IV)

Eight combinations of streptomycin (S), isoniazid (H), pyrazinamide (Z), ethambutol (E), and rifampicin (R) were in use in the study area. Most IDH + SANTA and CITY patients were treated with the SHZE regimen (62% and 59%, respectively). Most KDC patients were treated with the three-drug HZE regimen (67%). Only 26% of all patients (20,5 - 31,5%) received a rifampicin-containing regimen.

TABLE IV. THE MOST COMMONLY USED DRUG REGIMENS*

Kind of service	SHZE	R-regimen	HZE
IDH + SANTA	**62**	**31**	**2**
CITY	**59**	**18**	**18**
KDC	**12**	**14**	**67**
Border	**57**	**26**	**14**

*Percentage of patients
SHZE = streptomycin-INH-pyrazinamide-ethambutol; R-regimen = any regimen containing rifampicin; HZE = INH-pyrazinamide-ethambutol.

Main outcomes during management (Table V)

The diagnosis of pulmonary tuberculosis for 3% of patients was subsequently changed (denotified). Nineteen per cent were transferred out of the study area before treatment was complete. Four-and-a-half per cent of patients died, 3% being attributable to pulmonary tuberculosis; 16,5% were still attending for treatment after 15 months. The treatment of 1% of patients was stopped for medical reasons, and of 3% for non-compliance or behaviour unacceptable to the institution where they were being treated ('disciplinary' reasons). Twenty per cent stopped attending for no known reasons. Thirty-two per cent (26,5 - 37,5%) completed treatment within the study area.

TABLE V. MAIN CATEGORIES OF OUTCOME (%)

Incomplete data	**1**
Denotified – not pulmonary tuberculosis	**3**
Transferred out of the study area and not followed up	**19**
Died	**4,5**
Still attending for treatment after 15 months	**16,5**
Stopped attending	**20**
Treatment stopped prematurely for medical or 'disciplinary' reasons	**4**
Completed treatment	**32**
Total	**100**

Sputum conversion

From 1 month onwards after treatment began there was no information about sputum in 80% of patients (SANTA 58%, IDH 85%, CITY 89% and KDC 79%). Of the 8% of patients about whom there was sputum information at 5 months 4% were sputum-positive. Of the 20% of patients at SANTA about whom there was sputum information at 5 months 7% (4 cases) were sputum-positive.

Compliance with treatment (Fig. 3)

This analysis excluded denotified patients (3%) and patients transferred out of the study area and not followedup (19%). Of the remainder, 12% had incomplete data, had died or had their treatment stopped for medical or disciplinary reasons; 3,5% (1,5 - 5,5%) were early drop-outs; 10% (8 - 12%) were late drop-outs; 24% (18 - 30%) were infrequent attenders; and the remaining 50% (43 - 57%) were frequent attenders. Forty-one per cent (34-48%) were actually discharged from treatment of whom 63% were frequent attenders, 37% infrequent attenders and 99% had been treated for more than 12 months. Twenty-one per cent were still attending after 15 months.

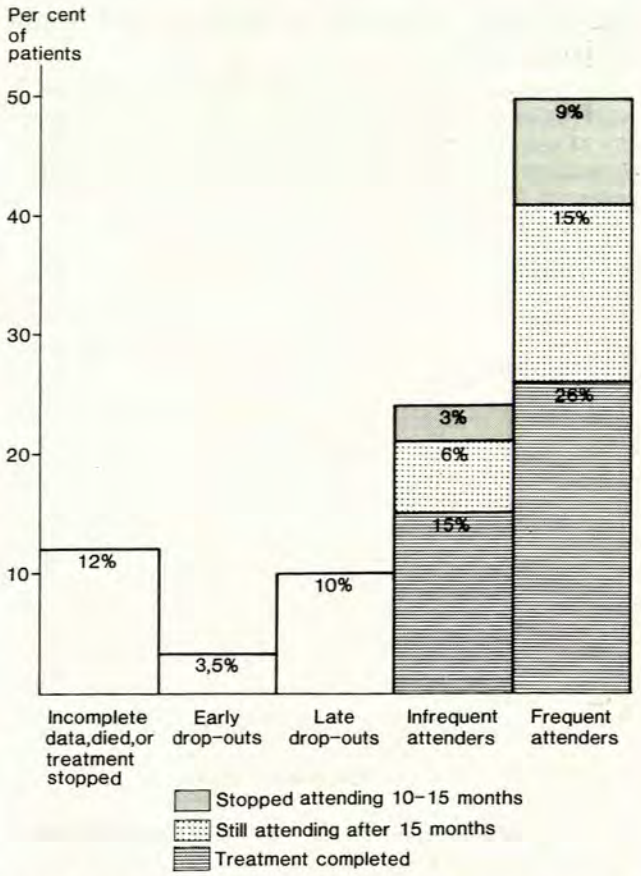

Fig. 3. Compliance with treatment. Patients who were denotified or transferred out of the study area are excluded.

Compliance of those initially hospitalised and those initially ambulant (Fig. 4)

Five per cent of the initially ambulant had incomplete data (3%), had died (1%) or had treatment stopped (1%). Eighteen per cent of the initially hospitalised died in hospital (10%) or had treatment stopped for 'disciplinary' reasons (8%). Early drop-outs in the initially hospitalised was 2,4% (0,3 - 8,3%) and in the initially ambulant 4,7% (1,4 - 8,0%). Frequent attenders in the initially hospitalised was 47% (36 - 58%) and in the initially ambulant 54% (46,5 - 61,5%).

Discussion

Age-specific incidence of pulmonary tuberculosis

The pattern of this estimate of the age-specific incidence of treated pulmonary tuberculosis and its peak (between 55 - 64 years) in the study area (Fig. 2) corresponded well with the pattern and peak (> 65 years) of age-specific notifications of

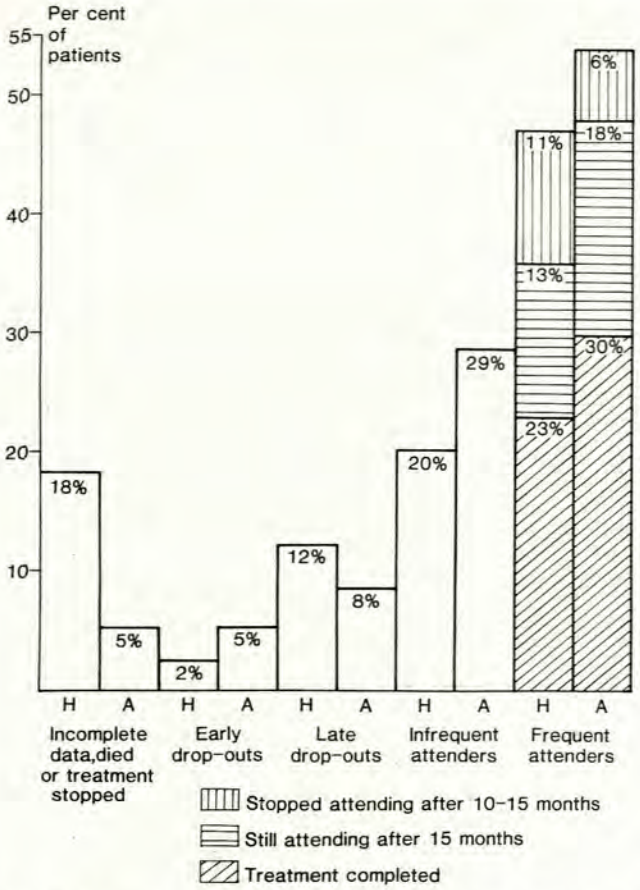

Fig. 4. Comparison of compliance between initially hospitalised (H) and initially ambulant (A) patients. Those denotified or transferred out of the study area are excluded.

pulmonary tuberculosis for 1983 in the eastern Cape (within which the study area falls) received by the Epidemiology Directorate, Department of National Health and Population Development (personal communication).

Previously treated patients

The proportion of patients in a treatment programme who have been treated previously, especially recently, is a rough index of prevailing relapse rates. The Department of National Health and Population Development reported in *Epidemiological Comments*[16] that 11% of new patients in the eastern Cape in 1985 and 1986 had had relapses or re-infections. In this study at least 37% of patients had been treated before, although not necessarily in the study area. If we reduce this by 20% — the proportion of patients we have judged, in retrospect, to be inactive and allow that half of these patients (those who had been treated before within 2½ years) were treatment relapses — then we may conclude that between 15% and 30% of patients had reactive pulmonary tuberculosis.

Diagnostic status

The Department of National Health and Population Development[17] found the question of how new cases were diagnosed disquieting; radiography and bacteriology had accounted at most for only 42%. In the study more than 99% of patients had had radiography and 92% had had at least one sputum examination (INH + SANTA 97,5%, CITY 90%, KDC 65%). The amount of *recorded* clinical information was scanty. We cannot tell in retrospect *how* the decision to treat was made; we can only consider the outcome.

Seventy-five per cent of patients were sputum-positive (INH + SANTA 87%, CITY 64%, KDC 31%) (Table II). Figures in Thomson and Myrdal's[13] study were 74% for hospitals, 43% for Cape Town clinics, and 22% for clinics in Ciskei. The figure in Fisher's[9] study for 2 Cape Divisional Council clinics was 72%.

Sputum-negativity, particularly under programme conditions, does not exclude active disease.[18–20] To use 70% or 50% probability as the criterion of activity in the radiographic review would change the proportion of all treated patients judged active to 4,8% or 9,4% respectively (unpublished data). Escreet and Cowie,[21] in a seminal article, allot the highest score for radiography (5), out of a diagnostic score of 10, for *cavitation* in upper or lower lobe apical segments. Very few of the radiographs reviewed showed cavitation.

However, the programme clinicians' responsibility was to decide whether or not to treat patients, which is also a probabilistic decision. But there is a strong tendency to simplify medical decision-making.[22] 'Anyone uncomfortable dealing with probabilities can use the heuristic: if there is any chance of (the disease), the (procedure) should be performed.'[22] Thus, important programme parameters can depend on personalised judgements. The final proportion of patients considered to have active disease was 81%. High as this proportion may seem, its real meaning is that 1:5 patients was treated unnecessarily. Furthermore 16,5% of patients, irrespective of initial sputum status, were still attending for treatment after 15 months.

The position regarding diagnostic criteria, summarised by Thomson and Myrdal,[23] is uncertain. The Department of Health and Welfare's 1979 Tuberculosis Policy Statement is only one of such that is non-committal. It is not surprising that, in the absence of agreed diagnostic criteria, operational standards for diagnostic efficiency have not been established.

Treatment delay

Aoki *et al.*[24] found that doctors' delay always exceeded patients' delay even when total delay exceeded 2 months. For those who underwent radiography at their first visit median doctors' delay was 13 days. Our estimate of median service delay in the Border region is the same, but the median service delay for the rural service was 4 weeks, and 10% of all patients had not begun treatment 5 weeks after radiography (Table II). Since the earliest encounter recorded in most patients was the date of radiography, we think these results are underestimates of health service delay. Such observations should temper the common criticism of patients' delay.

Drug regimens used

The impact of the 1979 Department of Health and Welfare Tuberculosis Policy Statement on rifampicin deployment was weakened because provision was not made for the financial and logistic implications.[25] The Department of National Health and Population Development[16] reported for the eastern Cape for 1985 and 1986 rifampicin usage of 84% and 83%, respectively. This study showed that in the Border region in 1983 less than one-third of patients received rifampicin. Supervision was implied in the Policy Statement as a prerequisite for its use, but this opportunity was not even exploited in hospitals, since only 32% of patients there received rifampicin. On the other hand, the difficulty of supervising daily or intermittent treatment in KDC is reflected in 67% of patients being on a 3-drug regimen (HZE). Although this regimen does not appear in the Policy Statement, Kleeberg[26] reported only 3% treatment failures and 4% relapses with it.

Main outcomes of management

The complexities of the diagnostic process, which are both clinical and logistic, may result in overtreatment of patients. A management programme that is properly aware of this will use therapeutic trials and patient reviews. We suggest that such programme sensitivity is reflected in denotification rates. In this study the rate was 3%.

Members of the health services in the study area at the time emphasised the management problems created by influx and efflux of patients from neighbouring Transkei and Ciskei. Nineteen per cent of patients were transferred out of the region before treatment was completed and their outcome is not known. This compares with 23% (32 patients) at SANTA and at a city clinic who were both born and domiciled in Transkei or Ciskei (unpublished observations). The Department of National Health and Population Development[16] did not report such an outcome category for the eastern Cape but reported for 1986 that 71% of black and coloured patients were cured and discharged, whereas we found that, even after excluding patients transferred out, the proportion completing treatment only increased from 32% to 41%.

Compliance

About 14% of patients stopped attending before 9 months, about 24% were infrequent attenders, and about 50% attended frequently. Sackett and Haynes[4] suggest that the *normal* pattern for compliance with long-term medication may be U-shaped in distribution with, for example, one-third of patients taking almost no medication, one-third taking almost all, and the rest scattered in between. Indeed Rouillon,[27] in a classic comment, thought that only an abnormal person would be coldly intellectual enough to swallow medicine every day. By comparison, this study population was unusually compliant, and 21% were still attending after 15 months! Unfortunately there is a tendency to treat the non-compliant as deviants. On the contrary, it is important that we think of highly compliant behaviour as unusual and therefore needing special motivation and support.

Dropping out from treatment need not be equated with treatment failure. Fox[28] and, in South Africa, Zabow and Pearson[29] have drawn attention to the probabilities of cure with modern ultra-short course regimens and the arresting of disease in patients who stopped attending after 40 - 80 doses. Also, as Sackett and Haynes[4] pointed out, some of those who drop out might be subjects who did not have active disease. Our samples were not large enough to infer this.

Sputum-conversion

With the powerful drug regimens now available, reduction in coughing and sputum production, and sputum-conversion are better indicators of response to treatment in the short-term than radiography. The paucity of information about sputum-conversion shows that insufficient importance was attached to this means of assessment. In 1983 76% of patients whose sputa were examined at the Frere Hospital regional laboratory were in hospitals and 11% were with local authority health services. Less than 1% were with the KDC (unpublished observations). We think that peripheral services feel disadvantaged with regard to laboratory services. There must be something awry if it is found easier to perform radiography in a rural patient than to examine the sputum.

Hospital v. clinic treatment

The Department of National Health and Population Development[16] reported that in 1985 and 1986 72% of all cases in the eastern Cape received treatment in clinics and 28% in hospitals as though these were separate populations. We found (Table I) that 62% of patients began treatment in hospital and 38% of patients began treatment as outpatients. There were no significant differences in compliance between the two groups, although the hospital group began with an assumed 100% compliance.

Conclusions

Our finding that about 19% of patients were treated unnecessarily shows how easily the diagnostic process can be compromised. Operational research, which is needed to improve the effectiveness of the Tuberculosis Control Programme, could establish standards for diagnostic efficiency.[30,31]

Other results of this study, which show important differences from the large-scale and cross-sectional data of the Tuberculosis Control Programme, were available 8 months after the study started. We think that local prospective cohort evaluation is necessary and feasible.

The study showed, not for the first time, a deficiency of laboratory information in the KDC for both diagnosis and monitoring of treatment response. Laboratory services are still regarded as a perk of central services instead of a way of strengthening otherwise disadvantaged peripheral services.

Supervised outpatient treatment using a 4-drug regimen, and rifampicin, where possible, has been State policy since 1979. Yet in the Border in 1983 62% of patients began treatment in hospital. The proportion of patients with active disease was considerably higher among the initially hospitalised than among the initially ambulant. Rifampicin was used in only 17% of outpatient regimens because of little opportunity to supervise treatment. An active transfer of resources to community services' infrastructure is imperative for ambulatory treatment to be successful.[31] Without sufficient of these resources the Border health services appear to some extent to have achieved treatment objectives better by hospitalising their patients.

What is wrong with the Tuberculosis Control Programme has become known in South Africa as 'the tuberculosis problem' and has been debated for years. The spread of operational research, which is really a management function, is confirming gaps between policy and implementation. Francis Peabody[32] said that the secret of the care of the patient is in caring for the patient. We conclude by echoing him: that the secret of better management of tuberculosis is to manage tuberculosis better.

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