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Patient Choice Promotes Adherence in Preventive Treatment for Latent Tuberculosis

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Abstract

Objective: To compare the effect of patient choice on completion rates and adverse drug reactions for patients treated for latent tuberculosis infection (LTBI) using 3-months rifampicin and isoniazid (3RH) or 6-months isoniazid (6H).

Methods: Data for all patients treated using 3RH or 6H for LTBI between 1998 and 2004 were analyzed.

Main results: 675 patients attended for chemoprophylaxis. 314 received 3RH and 277 received 6H. From 1st April 2000, patients were offered a choice of regimen. 53.5% successfully completed, a further 10.3% potentially completed and 36.2% failed to complete treatment. Logistic regression analysis suggested that successful completion was more likely in patients that were younger (an association lost after removing all those under 16 years), offered a choice of regimen and attended all clinics before commencing treatment. Treatment was discontinued due to adverse reactions in 16 (5.1%) patients prescribed 3RH and 16 (5.8%) prescribed 6H. Treatment failure was most likely for both regimens during the first 4 weeks of treatment. At 13 weeks treatment, more patients taking 6H had stopped compared to those completing the 3RH regimen. Drug costs were greater using 6H compared with 3RH.

Conclusions: Offering a choice of regimen improves completion. Most patients chose 3RH over 6H. Adverse drug reaction rates between the two regimens were similar.
Keywords: adherence; adverse effects; choice; isoniazid; latent tuberculosis; rifampicin

Introduction

Treatment of active tuberculosis should reduce incidence worldwide, but treatment of latent tuberculosis infection (LTBI) will be essential if tuberculosis is to be eradicated by 2050[1]. Isoniazid for 6-12 months has been the standard treatment for LTBI but there have been concerns over poor adherence and toxicity[2]. A randomized controlled trial in Hong Kong showed that 3 months of rifampicin and isoniazid was as effective as 6 months isoniazid in preventing tuberculosis[3] and retrospective data showed a significant reduction of paediatric tuberculosis from 1981-1996 at one site with this regimen[4]. Both six-month isoniazid (6H) and three-month combination of rifampicin and isoniazid (3RH) are accepted preventive treatment in the United Kingdom (UK)[5]. A recent meta-analysis suggested that the shorter regimen is as effective as longer regimens with isoniazid alone[6]. In the United States, initial promise of a two-month regimen of rifampicin and pyrazinamide proved to be associated with greater toxicity and has been abandoned[7]. A four-month regimen of rifampicin was explored in adolescents and was found to be effective[8;9].

In those who are asymptomatic but have a positive tuberculin skin test (PPD+)[2] and normal physical examination and chest x-ray, the risk of developing TB disease depends on immune competence[10] and BCG vaccination status[11]. In the UK, prior to recent NICE guidance[12], chemoprophylaxis was offered to PPD+ school children (no longer recommended), contacts, and young immigrants. Contacts of patients with pulmonary tuberculosis are screened for tuberculosis and those with a positive tuberculin response are recommended preventive treatment. Epidemiological evidence has shown that those

born in an area where tuberculosis is common are likely to develop disease within the following five years of residence in a low incidence country[13]. Therefore, new entrants to the UK are screened for tuberculosis and preventive treatment recommended for those with LTBI. Youth implies relatively recent infection and, hence, increased likelihood of developing disease. At the time of this study, BCG vaccination was recommended for school children aged 10-14 years in areas where tuberculosis was common. Those who had a positive tuberculin skin test were referred for further investigation rather than given the vaccine. The increased risk of serious adverse reactions to isoniazid has been estimated to outweigh the benefit in prevention of TB disease over age 35 years[14].

This study audited the adverse effects and adherence to two regimens of preventive treatment. In order to promote adherence, the effect of offering the choice of regimen to the patient was explored and a drug-cost comparison between the two regimens conducted.

Methods

Patient population. Patients at risk of LTBI residing in the London borough of Hackney attended an out-patient clinic in Homerton University Hospital. LTBI was defined as positive tuberculin skin test with a normal chest X-ray and inflammatory markers, and no clinical evidence of tuberculosis.

Preventive treatment. Adults 35 years or less were given either 6 months of isoniazid (6H) daily or 3 months with rifampicin (3RH). Children received isoniazid at 5 mg/kg body weight or in combination with rifampicin 10 mg/kg. Other regimens were

prescribed if 3RH or 6H were contraindicated or not tolerated. Until 1st April 2000, the decision regarding regimen was made by the attending physician. Thereafter, patients were invited to choose their preferred regimen. All patients had a measure of liver function made before start of treatment. Thereafter, any person with abnormal liver function and symptoms of hepatotoxicity had further investigation and the risks of proceeding with preventive treatment were explained on the basis of results. All patients and their families were given a leaflet describing common side-effects and TB clinic contact details if they experienced these.

Adherence and treatment outcome. Patients were invited to return to clinic two weeks after commencing chemoprophylaxis and report any problems with treatment. Thereafter, they were seen monthly to monitor adverse effects, adherence, and general wellbeing. Liver function tests were repeated if patients reported any symptoms. Preventive treatment was discontinued if AST or ALT levels were >100 IU/l[15]. Successful completion required attendance to all outpatient appointments with affirmative objective observations (urine tests) and evidence of tablet taking. Potentially successful completion was defined as a missed appointment or a single negative urine test fully explained by the patient, and sufficient medication supplied to ensure no gaps in treatment. Failure to complete included the remainder, i.e. those who defaulted from clinic without sufficient medication to ensure treatment completion.

Patient selection. To allow comparison between the mainstays of treatment, patients were selected for analysis if they had received 3RH or 6H regimens. Patients were excluded from analysis if they changed regimen during treatment (Table 1).

Data analysis. Epidemiologic data were collected routinely on all patients from 1998 to 2005. Data were coded and entered into SPSS® (version 12) database. Statistical association between completion rates and other variables was tested using contingency tables and Pearson's chi squared test (χ^2) for categorical data comparisons, and Mann-Whitney (*U*) or Kruskal-Wallis (*H*) test for categorical-continuous data. Variables that were significantly associated with outcome were entered into logistic regression analysis. To perform binary logistic regression, 'potentially successful' completion was categorized as 'failure' to create a dichotomous variable; successful completion in these patients cannot be assumed. Survival analysis was performed to compare completion failure for 6H and 3RH using Kaplan-Meier plot taking completion failure to represent "death". Duration of treatment was used as the survival time: minimum values calculated according to the last date a defaulting patient attended clinic and maximum values calculated from the duration represented by the total medication supplied to the patient. Failure rates were compared after 13 weeks using the Mantel–Haenszel test. A cost comparison of 6H and 3RH was conducted using recently reported drug costs. These drug costs were applied to the data-set to illustrate the 'real-life' situation as two different dosage regimes for the 3RH regimen had been used.

Results

Of the 675 patients that attended out-patient clinic, 84 were excluded from analysis (N=591, Table 1). Differences in demographic variables (age, gender, UK birth, and ethnicity) between those included and excluded from analysis were examined and demonstrated that patients excluded from analysis were more likely to have been born

outside the UK (n=593, nationality data missing for 64 patients: χ^2=6.19, p=0.013). Patients were not routinely followed up after completion of chemoprophylaxis but one patient developed lymph node TB after completion; a male Vietnamese immigrant with isoniazid-resistant TB. Mean age of patients was 22.5 years and more males (61.9%) than females were treated, which were comparable to our local TB population aged less than 35 years (mean age = 23.7 years, unpublished data).

Most patients attending clinic (n=586, Table 2) were either referred as new arrivals to the UK (49.3%) or as contacts of an infectious TB case (42.2%), with a smaller proportion of school referrals (8.5%); five patients were referred through different channels. Predictable differences were observed between the three main referral routes, for example, school reactor patients were more likely to be younger (Table 2).

Slightly more patients received 3-month rifampicin/isoniazid regimen (3RH: n=314, 53.1%) than 6-month isoniazid (6H). Slightly fewer patients were offered a choice of which regimen they were prescribed (i.e. offered after 1st April 2000; n=287, 48.6%). When offered choice (n=287), most patients chose 3RH (78.7%) over 6H. All 591 patients were assigned treatment completion outcomes: 53.5% successfully completed treatment, 10.3% potentially successfully completed treatment, and 36.2% failed to complete treatment.

Analyses indicated that younger patients, those prescribed 3RH regimen, those offered a choice of regimen, those attending all clinics before commencing treatment, and those

treated more recently were more likely to achieve successful completion (Table 3). Analyses using just the two outcome categories 'success' and 'failure', separately, and combining 'potential success' into 'failure' were similar and justified the categorisation of 'potential success' into 'success' and entry of the variables above into binary logistic regression. Three variables – age, choice of regimen and attendance to clinic before treatment – significantly contributed to a model predicting completion outcome (Table 4). This suggested that for each year of age, patients were 1.04 times more likely to fail completion, patients attending all clinics before commencing treatment were 0.54 times more likely to fail, and if patients were offered a choice of treatment regimen they were 0.43 times more likely to fail. Further investigation of age and completion outcome demonstrated that when patients under 16 years were excluded, the association between these two variables was lost (Kruskal Wallis Test: χ^2=0.53, p=0.77).

As Kaplan-Meier plots displaying minimum and maximum possible durations of treatment exhibited similar results, only the graph displaying minimum duration is shown (Figure 1). Survival analysis demonstrated differences in failure rates between regimens summarized as follows: 1) The highest probability of failure was at the beginning of treatment for both regimens (χ^2 test, p<0.001); 2) the probability of failure at any one time decreased throughout treatment for both regimens; 3) at 13 weeks, when 3RH regimen had ended, the probability of failure was significantly greater for 6H regimen (Mantel–Haenszel test, p<0.001).

Thirty-two (5.4%) patients had their treatment stopped by the attending physician due to symptoms of hepatotoxicity (Table 5); 16 had been prescribed 3RH regimen (5.1%) and 16 had been prescribed 6H (5.8%). These rates were not significantly different (χ^2 test, p=0.84). Of the patients taking isoniazid, twelve (75%) stopped treatment in the first 3 weeks and of those taking 3RH twelve (75%) stopped treatment in the first month. Transaminase levels never exceeded five times the upper limit for either regimen. Symptoms resolved for 26 patients whose AST/ALT levels were initially elevated and treatment was then safely continued at the request of the patient.

Basic drug costs of the two regimens, based on current prices, were compared (Table 6) excluding patients receiving variable dose regimens (n=34) and whose dose/formulation was changed during treatment (n=21). The drug cost per patient treated for the entire duration was greater using 6H (£103.86) compared with 3RH for both dosing schedules (£49.65 – £65.61). When these costs were applied to the current data-set to demonstrate costs for the past seven years treatment, the cost per patient prescribed 6H was 1.6 times more expensive compared with 3RH. In addition, due to the longer duration of treatment using 6H, patients would have needed to attend two extra clinics resulting in a further cost implication.

Discussion

This study describes data from a diverse patient cohort who were under greater threat of developing TB disease. Over the 7-year timeline, the overall non-adherence rate was high. Between 36% and 47% of patients did not successfully complete treatment and high

rates of non-attendance to clinic were observed before commencing treatment. Offering a choice of regimen resulted in improved completion outcomes; the majority of patients chose the shorter regimen (3RH). The two regimens had similar adverse drug reaction profiles and average drug cost of using 3RH was considerably less than 6H.

In the current study setting different indicators of adherence were used. Objective urine tests were used in conjunction with patient reported adherence and clinic attendance to guide clinicians in assigning completion outcomes. Assessing adherence using a combination of objective and subjective tests has been recommended[16]. Failure of treatment completion generally represented those patients who had defaulted from treatment. This demonstrates high levels of non-adherence (36-47%) in this cohort and may relate to the preventive nature of treatment amongst asymptomatic patients. Non-attendance to clinic was also high before commencing chemoprophylaxis (31%), revealing poor commitment to health services. The rates of treatment completion of the trials (67-100%) reported in a meta-analysis may be superficially high due to the effects of trial intervention[6]. For example, consistently high rates of completion (95.2-96.5%) were reported in one of the included clinical trials[3]. Besides the effect of trial intervention other differences may exist between reported trials and the current study. For example, the Hong Kong trial recruited silicosis patients from a Chinese population in which 98% of patients were aged over 34 years[3]. Therefore, a comparison of the current study with clinical trials may be unwarranted. Lobue and Moser[17] reported lower successful completion rates of 64% in a large retrospective study (N=3788). In the present study if successful and potentially successful completion outcomes are combined

then results are similar (~64% completion). Nevertheless, as effective drug prevention of TB relies on treatment of large cohorts, resources should be concentrated to improve the adherence rates in this setting.

Until 1st April 2000, patients were generally prescribed 6H, unless contraindicated. After this date, a choice between 6H and the newly recommended 3RH was offered. The vast majority of patients (86%) chose 3RH over 6H when offered a choice. Reichman et al[18] similarly observed that patients commonly opted for a shorter regimen, 4-month rifampicin in their case, over longer duration regimens such as 6- or 9-month isoniazid.

The present study used logistic regression to demonstrate that younger patients, those offered a choice of regimen, and those that did not miss a scheduled clinic before commencing treatment were more likely to complete treatment. However, analysis of the data excluding those under the age of 16 years failed to show an effect of age on outcome. The higher success rate amongst younger patients may indicate greater social support in this group: children probably had greater supervision at home in addition to that provided by the TB clinic. Offering choice of which regimen patients received increased the likelihood of successful completion outcomes over and beyond any positive effect of either regimen. This finding appears to support the argument for a concordant relationship between patients and prescriber[19]. Finally, the attendance of patients before commencing treatment appears to be important corroborating earlier findings that non-adherence is likely to be persistent[20].

Survival analysis allowed a comparison between treatment regimens of default rates over time (duration of treatment). Patients prescribed 6H had a higher probability of failure compared with those prescribed 3RH combination. For both regimens, the highest failure rates occurred at the beginning of treatment. Patients prescribed 6H continued to fail after three months. Patients may struggle to commit to a lengthy preventive treatment which does not result in a tangible benefit to the patient, for example, in reducing symptoms. The finding that default rates are highest in the early stages of treatment has similarly been observed elsewhere[21;22]. This infers that intervention to address this should be concentrated on this initial period, while patients may be adjusting to the routine of their medical management. The data show that adherence continues to fall over time implying that a shorter regimen is more beneficial.

In the current study, the adverse drug reaction rates requiring treatment discontinuation were similar (3RH = 5.1%, 6H = 5.8%). In their meta-analysis of five randomized controlled trials (N=1926), Ena and Valls[6] also found similar rates of adverse reactions requiring treatment discontinuation between comparable regimens (3RH = 4.9%, ≥6H = 4.8%). There was, however, wide variation in rates between studies included in the meta-analysis (3RH, 2-18%; ≥6H, 1-24%). Nolan et al[23] investigated the rate of hepatotoxicity in patients prescribed isoniazid preventive treatment (N=11,141). Of the eleven episodes of hepatotoxicity reported, ten (91%) occurred within the first three months of starting treatment. If these results are generalisable to other patient populations, and apply to other regimens, then shorter regimens, such as 3RH, may not achieve a clinically significant reduction in adverse reaction rates. In the current study,

most patients also had their treatment stopped due to adverse reactions in the early stages of treatment: 75% of patients taking isoniazid had their treatment stopped within the first three months, and 75% of patients taking 3RH had their treatment stopped within the first month.

Based on simple drug costings using current prices, 6H was found to be 1.6 times more expensive than 3RH. This implies that for the average number of patients treated in a year in Hackney (n=91), 55 more patients could be treated using 3RH than 6H for the same cost. This is a conservative estimate as it does not take into account costs of extra clinics attended by patients treated using 6H due to the longer duration of treatment. More sophisticated models comparing directly observed therapy and including patient costs are being developed.

Approximately 10% of patients infected with TB are estimated to develop disease at some point in their lifetime[11;24]. To achieve the most significant public health impact in TB prevention, chemoprophylaxis relies on the greatest number of eligible patients accepting and completing treatment. It is unrealistic to expect absolute acceptance of and adherence to preventive treatment of long duration. Therefore, efforts have been focused on establishing shorter preventive regimens. Results from logistic regression analysis demonstrated that the only alterable variable that contributed to the final model in predicting treatment completion was patient choice of regimen. This suggests that any intervention introduced should be based on offering greater choice to LTBI patients rather than the promotion of one particular regimen necessarily. Nevertheless, 3RH was

shown to be equivalent to 6H in terms of adverse reactions and favourable in terms of patient preference and treatment duration. Therefore, wider adoption of 3RH regimen should seriously be considered elsewhere until shorter, more efficacious, regimens are identified.

A number of limitations to this study are evident. Better reporting of data on sociological variables may have elucidated whether social support was an important factor affecting treatment completion outcomes. Future research should include a detailed assessment of patient sociological status as well as demographic variables that may impact on the process and outcome of latent TB management, with particular reference to early defaulting. This study was pragmatic and sequential and, therefore, retrospective and uncontrolled. In addition, as the study was not blinded there can be no accounting for clinician bias, for example, whether patients offered choice received greater explanation by clinician. However, patient information was delivered by the whole TB staff team, not just the clinician, and it is unlikely that information delivered altered in any way, given that patients received both regimens before choice of regimens was offered. A randomized controlled trial to compare 3RH and 6H regimens, or offering choice of regimens, has ethical problems. It would not be fair to offer choice to some patients but not others. Similarly, to constrain patients to a longer regimen (6H) that has no proven benefit and is evidently less preferable would also be unfair. This study did not have the power to evaluate how effective regimens were in preventing TB. Finally, a more detailed economic analysis is being undertaken.

In conclusion, patient choice of preventive treatment for TB significantly improves adherence and early defaulting requires investigation.

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Table 1: Description of inclusion and exclusion of patients in analysis

Patient inclusion in analysis	**N**
Patients potentially eligible for chemoprophylaxis	**675**
Patients excluded from analysis:	**84**
Patients prescribed regimens other than 3RH or 6H	11
Regimens changed during treatment	26
Prophylaxis refused by patients	11
Patients transferred to another clinic	12
Patients with TB other than LTBI	10
Prophylaxis not intended	4
Patients absconded before being offered prophylaxis	4
Patients discharged with X-ray follow-up	3
Patients not prescribed prophylaxis due to age (>35 years)	2
Prophylaxis contraindicated – high liver transaminase levels	1
Patient data entered for analysis of comparison between regimens:	**591**
Patients referred as new arrivals	289
Patients referred as contacts	247
Patients referred as school reactors	50
Other referral (e.g. self-referral)	5

Definitions of abbreviations: RH = rifampicin/isoniazid, H = isoniazid, LTBI = latent tuberculosis infection

Table 2: Demographic and treatment characteristics of referral groups

Variable*	New Arrivals (n=289)	Referral Contacts (n=247)	School Reactors (n=50)	Total (n=586)
Age (mean)†	25.4	20.9	12.9	22.5
Gender (% male)‡	69.2	56.3	48.0	61.9
Country of birth (% UK born)†	0	39.8	52.0	21.2 (n=585)
Ethnicity (n)†				
White UK	0	26	10	36
White EU	26	11	0	37
White non-EU	82	44	8	134
Asian ISC	43	32	8	83
Southeast Asian/Chinese	26	13	3	42
Black	91	91	21	202
Black Somali	9	28	0	37
Middle Eastern/Arab	12	2	1	15
Spoken language (% English)†	31.6	68.7	98.0	52.5 (n=568)
GP (% registered)†	68.1	81.4	90.0	75.6 (n=585)
BCG (% vaccinated)	78.7	75.9	68.0	76.6 (n=578)
Clinic attendance pre-treatment (% DNA)	32.5	24.3	24.0	28.3
Regimen choice (% offered)	50.2	46.6	50.0	48.6
Regimen prescribed (n)				
RH	168	125	19	312
H	121	122	31	274
Treatment restart (% restart)	11.1	8.1	18.0	10.4
Regimen change (% change)	1.7	6.5	2.0	3.8
Completion outcome (%)				
Success	52.9	52.2	64.0	53.6
Failure	34.6	40.5	22.0	36.0
Potential success	12.5	7.3	14.0	10.4

Definition of abbreviations: UK = United Kingdom, EU = European Union, ISC = Indian Sub-Continent, GP = General Practitioner, DNA = Did not attend, RH = rifampicin/isoniazid, H = isoniazid.

*Statistical significance; all tests performed using Pearson chi-squared (χ^2) except age comparison using Kruskal-Wallis Test (*H*).

†$p<0.001$; ‡$p<0.01$

Table 3: Association between completion outcomes and variables

Variable*	Outcome			Total (N=591)
	Success (n=316)	Failure (n=214)	Potential success (n=61)	
Age (mean) ‡	21.1	23.7	25.2	22.5
Gender (% male)	60.1	62.1	73.8	62.3
Country of birth (% UK born)	77.5	78.4	83.6	78.4
Ethnicity (n)				
White UK	23	13	2	38
White EU	18	16	3	37
White non-EU	80	44	13	137
Asian ISC	48	27	8	83
Southeast Asian/Chinese	29	11	2	42
Black	98	76	28	202
Black Somali	12	21	4	37
Middle Eastern/Arab	8	6	1	15
Spoken language (% English)	52.8	55.5	42.6	52.7
GP (% registered)	78.7	70.6	78.7	75.8
BCG (% vaccinated)	75.2	79.3	74.6	76.6
Clinic attendance pre-treatment (% DNA) †	20.9	37.4	34.4	28.3
Regimen choice (% offered) †	58.5	35.0	44.3	48.6
Regimen prescribed (n) †				
RH	189	86	39	314
H	127	128	22	277
Treatment restart (% restart)	8.9	10.3	18.0	10.3
Regimen change (% change)	0.3	0	0	0.2
Year (% with each year) †				
1998	43.4	47.6	9.0	100
1999	39.7	47.1	13.2	
2000	51.7	37.1	11.2	
2001	67.4	24.2	8.4	
2002	51.5	35.3	13.2	
2003	78.3	15.2	6.5	
2004	72.2	13.9	13.9	

Definition of abbreviations: UK = United Kingdom, EU = European Union, ISC = Indian Sub-Continent, GP = General Practitioner, DNA = Did not attend, RH = rifampicin/isoniazid, H = isoniazid.

*Statistical significance; all tests performed using Pearson chi-squared (χ^2) except age comparison using Kruskal-Wallis Test (*H*).

†$p<0.001$; ‡$p<0.01$

Table 4: Model variables predicting completion outcome

Variable	Wald statistic (χ^2)*	AOR (95% CI)
Age (continuous variable)	15.5	1.04 (1.02-1.06)
Clinic attendance before treatment	10.4	0.54 (0.37-0.78)
Choice of regimen	23.3	0.43 (0.30-0.60)
Constant	0.3	NA

Adjusted odds ratio (AOR) and 95% confidence intervals (CIs) were calculated using binary logistic regression and all variables entered by forward stepwise method. *Wald statistic identifies variables that significantly contribute to the model: All entered variable *p* values for Wald statistic were <0·01; constant *p*=0.56. Nagelkerke R^2 for the model is 0.12. NA = not applicable.

Table 5: Characteristics of patients who had treatment stopped due to adverse reactions

	Ethnicity	Gender	Age	Regimen	Side effects reported	Elevated AST*	Elevated ALT*
1	White-UK	Female	3	H	Vomiting	✓	✓
2	White-UK	Female	15	H	Urticarial rash		
3	White-UK	Male	2	H	Clumsy		✓
4	White-UK	Male	13	H	Back pain		
5	White EU	Female	26	RH	Nausea, dizziness		
6	White EU	Female	30	RH	Acute anaphylaxis		
7	White non-EU	Female	31	H	Reaction to H		
8	White non-EU	Male	24	H	Mania		
9	White non-EU	Male	32	RH	Limb pain, dizziness		
10	White non-EU	Male	31	RH	Hay fever nausea		
11	White non-EU	Male	10	H	Dizziness, sickness		
12	White non-EU	Male	32	RH	Hepatitis		
13	White non-EU	Male	35	H	Severe itchy skin rash		
14	White non-EU	Female	31	H	Itch, swollen hands		
15	White non-EU	Male	30	H	Vomiting		
16	Asian ISC	Male	24	RH		✓	
17	Asian ISC	Male	20	RH	Dry mouth		
18	Asian ISC	Male	30	H	Vomiting	✓	
19	Southeast Asian/Chinese	Male	32	H	Pain		
20	Southeast Asian/Chinese	Male	11	H	Itching		
21	Black African	Male	29	RH			
22	Black African	Female	29	RH	Sleep disturbance		
23	Black African	Male	28	RH	Mania		
24	Black Afro-Caribbean	Female	17	H	Dizziness, nausea		
25	Black African	Female	29	H	Nausea	✓	
26	Black African	Female	33	RH	Itching		
27	Black African	Male	22	RH		✓	
28	Black African	Male	31	RH			
29	Black Somali	Female	26	RH	Nausea		
30	Black Somali	Female	23	RH	Dizziness		
31	Arab/Middle Eastern	Male	24	H	Indigestion		
32	Arab/Middle Eastern	Male	33	RH	Itching		

* AST or ALT levels >40 IU/l

Table 6: Drug-cost comparison of 6H and 3RH

Drug regimen	1-month pack price*	Cost for regimen duration	Number of patients treated[#]	Drug cost per patient	Clinic number[¤]
6H (3×100mg)	£17.31 (3×28 tablet pack)	£103.86	260	£103.86	5
3RH (3×150/100mg)	£16.55 (1×84 tablet pack)	£49.65	24	£64.26	3
3RH (2×300/150mg)	£21.87 (1×56 tablet pack)	£65.61	260		

*Prices calculated from current prices reported in the British National Formulary, 52nd edition, September 2006.
[#]Excluded patients: those not receiving fixed dose regimens (n=34) and those whose dose or formulation was changed during treatment (n=21). [¤]Number of clinics scheduled for patients after commencing treatment.