



# Evaluation report: A Community Pharmacy Tuberculosis Medicines Compliance Scheme, Cwm Taf Health Board

**Author:** Sian Evans, Principal Pharmacist in Public Health

**Date:** 3 April 2012

**Version:** Final

**Publication/ Distribution:**

- Public Health Director, Cwm Taf Health Board
- Respiratory Team, Royal Glamorgan Hospital
- Health Protection Division, Public Health Wales
- Public Health Directors, Health Boards
- Chief Pharmacists, Health Boards
- Chief Pharmaceutical Officer , Welsh Government

**Purpose of document:**

To report an evaluation of a new *Community Pharmacy Tuberculosis Medicines Compliance Scheme*. This was developed in response to a screening initiative in small deprived community in Cwm Taf.

## Table of contents

|           |                                                    |           |
|-----------|----------------------------------------------------|-----------|
| <b>1</b>  | <b>SUMMARY .....</b>                               | <b>4</b>  |
| <b>2</b>  | <b>INTRODUCTION .....</b>                          | <b>4</b>  |
| <b>3</b>  | <b>PURPOSE .....</b>                               | <b>5</b>  |
| <b>4</b>  | <b>BACKGROUND .....</b>                            | <b>5</b>  |
| 4.1       | Epidemiology .....                                 | 6         |
| 4.2       | Pharmacotherapy .....                              | 7         |
| 4.3       | The screening initiative .....                     | 7         |
| 4.4       | Service provision.....                             | 8         |
| <b>5</b>  | <b>AIMS AND OBJECTIVES.....</b>                    | <b>9</b>  |
| 5.1       | Aim .....                                          | 9         |
| 5.2       | Objectives .....                                   | 9         |
| <b>6</b>  | <b>METHOD.....</b>                                 | <b>9</b>  |
| 6.1       | Literature review .....                            | 9         |
| 6.2       | Data collection.....                               | 9         |
| 6.3       | Ethics approval .....                              | 11        |
| 6.4       | Evaluation framework .....                         | 11        |
| 6.5       | Population under study .....                       | 11        |
| 6.6       | Exclusion criteria.....                            | 11        |
| <b>7</b>  | <b>KEY FINDINGS .....</b>                          | <b>12</b> |
| 7.1       | Literature review .....                            | 12        |
| 7.2       | Patients identified with TB through screening..... | 13        |
| 7.3       | Patients included in the evaluation.....           | 13        |
| 7.4       | Demography .....                                   | 13        |
| 7.5       | Effectiveness .....                                | 15        |
| 7.6       | Efficiency .....                                   | 16        |
| 7.7       | Accessibility and acceptability .....              | 17        |
| 7.8       | Other themes identified during interview .....     | 20        |
| <b>8</b>  | <b>DISCUSSION .....</b>                            | <b>21</b> |
| 8.1       | Limitations .....                                  | 22        |
| 8.2       | Lessons learned .....                              | 24        |
| <b>9</b>  | <b>CONCLUSION .....</b>                            | <b>25</b> |
| <b>10</b> | <b>REFERENCES.....</b>                             | <b>26</b> |

| <b>Appendices</b> |                                                                                          |
|-------------------|------------------------------------------------------------------------------------------|
| <b>Appendix 1</b> | Service specification of the Community Pharmacy Tuberculosis Medicines Compliance Scheme |
| <b>Appendix 2</b> | Literature review method and search strategy                                             |
| <b>Appendix 3</b> | Summary table of literature critically appraised                                         |
| <b>Appendix 4</b> | The pathways and completion status of the intention to treat population                  |
| <b>Appendix 5</b> | Summary of costs used for the Cost Effectiveness Analysis                                |

|                 | <b>Index of figures</b>                                                       | <b>Page</b> |
|-----------------|-------------------------------------------------------------------------------|-------------|
| <b>Figure 1</b> | Rates of active TB infection in UK 2000-2009                                  | <b>5</b>    |
| <b>Figure 2</b> | Number of active TB cases (and rates) in Wales 1999-2009                      | <b>5</b>    |
| <b>Figure 3</b> | Graph illustrating gender by age group of patients included in the evaluation | <b>13</b>   |

|                | <b>Index of tables</b>                                                                                                 | <b>Page</b> |
|----------------|------------------------------------------------------------------------------------------------------------------------|-------------|
| <b>Table 1</b> | Breakdown of gender (by age group) of patients included in the evaluation                                              | <b>13</b>   |
| <b>Table 2</b> | Breakdown of gender (by age group) of patients accessing services                                                      | <b>13</b>   |
| <b>Table 3</b> | Breakdown of place of residence for patients accessing the two services in the evaluation                              | <b>14</b>   |
| <b>Table 4</b> | Breakdown of the number and treatment completion of patients accessing the community pharmacy and the hospital service | <b>14</b>   |
| <b>Table 5</b> | Rate ratio of the completion rates                                                                                     | <b>15</b>   |
| <b>Table 6</b> | Summary of direct costs used for cost effectiveness analysis                                                           | <b>16</b>   |
| <b>Table 7</b> | Breakdown of patients interviewed                                                                                      | <b>17</b>   |
| <b>Table 8</b> | Breakdown of stakeholders interviewed                                                                                  | <b>17</b>   |

## 1 Summary

- As a result of an ongoing outbreak of tuberculosis, in a small village in south Wales, a community screening initiative took place.
- Consequently a new *Community Pharmacy Tuberculosis Medicines Compliance Scheme* was piloted.
- A cohort of patients accessed a community pharmacy for the supply and management of medication for latent tuberculosis. A separate cohort of patients accessed usual care provided by the hospital respiratory team. This occurred by chance and was not designed as a randomised control trial.
- The community pharmacy service reported 75% (n=6) of patients completing treatment compared with 20% (n=1) by the hospital service.
- Results indicate that the community pharmacy service was more effective than the hospital service (rate ratio 3.75, 95% CI 0.62-22.64) but this was not statistically significant (p=0.103).
- The community pharmacist service was found to be the more cost effective service (cost per treatment completed £91.13 compared with £490.05 for the hospital service).
- Patients and stakeholders found the community pharmacist service accessible and acceptable.
- The model could be considered for future TB medication services. It can also be adopted for use with other medical conditions or diseases requiring close monitoring of treatment and adherence to medication.

## 2 Introduction

Adherence to prescribed medication is an essential part of managing patients' medical conditions and diseases. Prescribed medications can only be effective if they are taken as indicated.

Non-adherence is a problem worldwide and in the UK has been reported to be as high as 50% for patients with long term conditions.<sup>1,2</sup>

For conditions such as communicable diseases, non-adherence to treatment in an individual can have consequences on the control and spread of infection in the wider population. Non-adherence therefore affects not only the individual but local populations and society as a whole.<sup>2,3,4</sup>

It is important therefore, if treating individuals with medication to provide effective services to support their adherence to medication.

This evaluation describes how a community pharmacist provided an adherence service to a group of patients with latent tuberculosis via the local community pharmacy.

### 3 Purpose

To report the findings of an evaluation of a new community pharmacy service titled *The Community Pharmacy Tuberculosis (TB) Medicines Compliance Scheme* which was developed in response to a screening initiative in a small deprived community in Cwm Taf.

### 4 Background

In 1996 there was an outbreak of active pulmonary tuberculosis infection in a small community in Cwm Taf. The outbreak consisted of seven cases, all amongst young people, which resulted in three deaths. One death was in a pre-school child.

Despite ongoing contact tracing, screening and treatment of individuals with tuberculosis (TB), cases of active TB in the particular community continued to be reported.

To date 26 cases of active TB have been reported in area. All 26 active TB cases have been linked by common contacts. Advances in DNA typing over recent years have confirmed that the 26 cases were the same strain of TB as the original 1996 cases.

A review of the situation in 2008 prompted the preparation of a screening initiative. The intention was to identify and treat individuals with active and latent TB in this community.

The community in question is a small village situated in the borough of Cwm Taf in the south Wales valleys. The close knit community hosts a predominantly white indigenous population of approximately 4000 people. The village is located 14 miles north of the capital Cardiff and although the nearest town is two miles away, the village is somewhat remote and isolated.

The community consists largely of a post war council housing estate and is classed as an area of high deprivation. The electoral ward is ranked the 30th most deprived ward of 1,896 wards in Wales (Public Health Wales Observatory 2011)

Amenities in the village are limited with a church, primary school, corner shop, community centre, social club, branch GP surgery and a community pharmacy which also hosts a post office. Lack of car ownership and no rail links means the nearest town of Pontypridd can only be accessed by bus. The nearest hospital offering routine services is 8 miles and two bus rides away.

This is an area of high unemployment and low income. Some individuals may not be able to afford the transport to access amenities regularly that are not locally available. This makes some members of the community very isolated.

## 4.1 Epidemiology

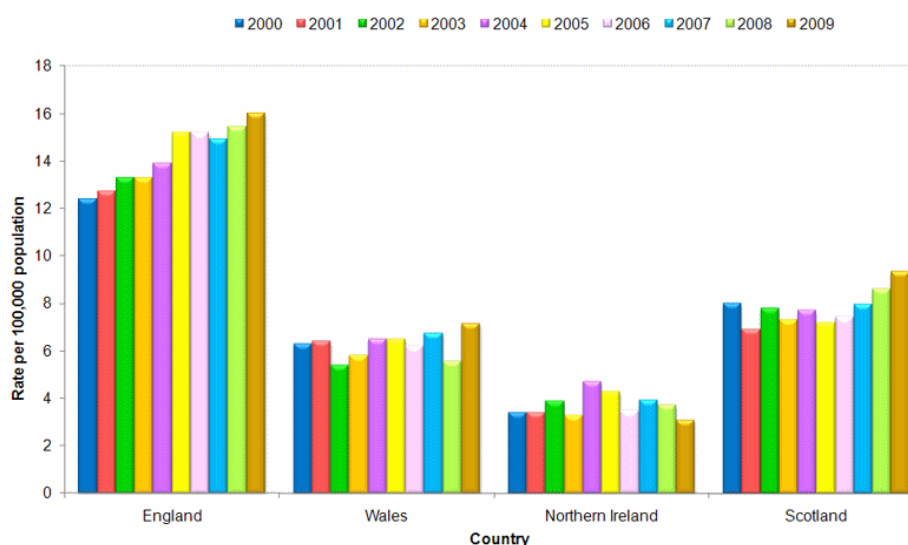
Tuberculosis is caused by the bacterium *Mycobacterium tuberculosis*. It mostly affects the lungs (pulmonary) but can affect other parts of the body.<sup>5</sup>

Tuberculosis can be active or latent. Individuals with latent TB do not experience any symptoms and therefore are often unaware of their condition. The infection may develop into active TB anytime after first contracting the infection or can remain inactive (latent) throughout their lifetime.<sup>5</sup> It is anticipated that up to 10% of people with latent TB, and no other complications will develop active TB in their lifetime.<sup>6,7</sup>

People who have latent TB cannot spread the infection whilst individuals with active TB can pass the bacteria to anyone they come into prolonged close contact with commonly through coughing and sneezing.<sup>6</sup> The presentation of active TB is usually when an individual's immune system becomes weakened. Symptoms include coughing (sometimes coughing up of blood), chest pains, fatigue, weight loss, chills, fever and night sweats.<sup>8</sup> If untreated it is possible that one person with active TB will infect on average between 10 and 15 people with TB every year.<sup>7</sup>

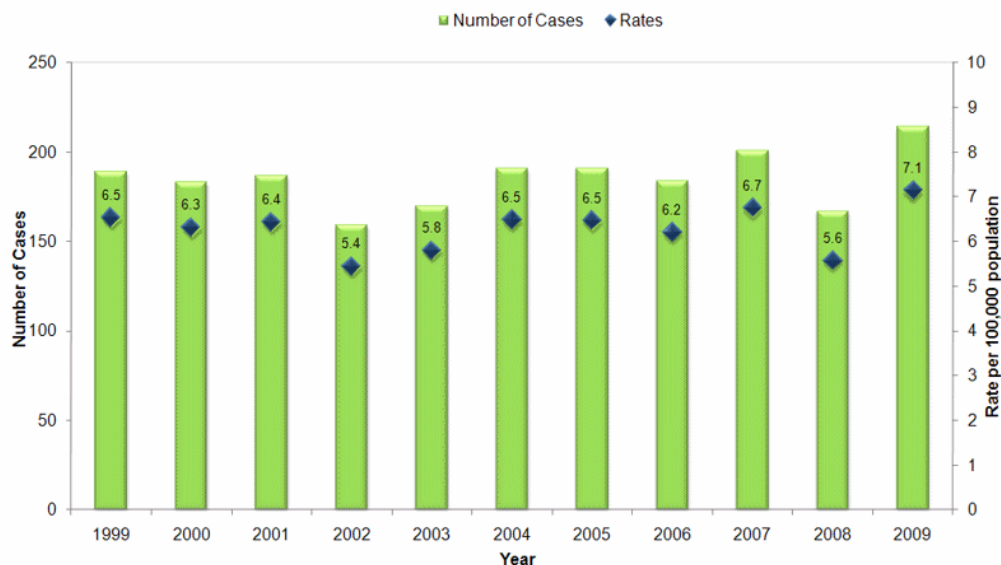
Across the UK, and in Wales, TB is relatively uncommon. Approximately 180 active TB cases are reported annually in Wales.<sup>9</sup>

Generally the rate of TB is lower in Wales than that reported in England and Scotland but greater than the rate in Northern Ireland.<sup>9</sup>



**Figure 1: Rates of active TB infection in UK 2000-2009**

The number of active TB cases in Wales has remained relatively constant over the last 10 years (figure 2). In 2009 however a record 214 cases of active TB were reported in Wales.<sup>9</sup>



**Figure 2: Number of active TB cases (and rates) in Wales 1999-2009\***

## 4.2 Pharmacotherapy

Both active and latent tuberculosis are treated with one of a number of recommended antibiotic regimes. All regimes have reported unpleasant adverse effects and intolerance to these can affect treatment completion.<sup>10</sup> As individuals with latent TB experience no symptoms, it is possible that adherence to a treatment with noted adverse effects for a number of months is a challenge and can lead to treatment incompleteness.

Chemoprophylaxis for latent TB consisted of a daily treatment regime of 600mg rifampicin plus 300mg isoniazid as a combination preparation known as Rifinah<sup>®</sup>. The recommended adult dose was prescribed as two Rifinah<sup>®</sup> 300 / 150 tablets daily.<sup>10,11</sup>

## 4.3 The screening initiative

In March 2010, a series of targeted screening events were held in the local church in the community. It was the first of its kind in Wales.<sup>12</sup>

Screening was predominantly targeted at known close contacts. Individuals identified as close contacts since 1996 were invited by letter to attend for screening for latent and active TB. Individuals who presented opportunistically at the events were also offered screening. The event was widely publicised by community leaders, local and national press and the media.<sup>12</sup>

Screening by Mantoux testing was offered to all those presenting.<sup>12</sup> Following subsequent testing and chest x-rays, 21 patients were confirmed to have latent TB and were eligible for treatment according to clinical guidelines.<sup>13</sup>

No active TB cases were found through the screening events. Two cases of active TB however were identified in this community in 2010 presenting at the GP surgery as a result of the heightened awareness of the symptoms of TB in this population.

#### 4.4 Service provision

Patients identified with TB in the Cwm Taf locality usually access the hospital led TB service provided by the respiratory team based at the Royal Glamorgan Hospital in Llantrisant. This service is led by a consultant and a team of respiratory nurses. One nurse has a specialist interest in TB (the TB specialist nurse). All tests and diagnostics are usually performed at the hospital and medication supplied from the hospital pharmacy. Medicines are usually dispensed as a single three month supply.

It was unknown how many people would present for the local screening events in 2010 and consequently how many people would be identified with TB and require treatment. The capacity for the hospital service to manage a large number of patients with TB, if this was the case, became cause for concern.

A new treatment service model, the **Community Pharmacy Tuberculosis Medicines Compliance Scheme** was developed to minimise capacity pressures and to test a new service model (Appendix 1). The service was to be provided by the local community pharmacist located in premises on the main council estate in the centre of the community.

The community pharmacy service was delivered with support from the respiratory team (RGH). The TB specialist nurse provided telephone contact to advise and support the pharmacist and patients with specific issues where non-adherence was suspected.

Patients initially attended a community assessment clinic, held in the local church, where they were reviewed by the TB specialist nurse and prescribed medication by the respiratory consultant. Medication was prescribed by the consultant using WP10HP prescriptions.

A series of WP10HP prescriptions for each patient to cover 3 months duration were written and supplied to the community pharmacy at the start. Each prescription enabled the community pharmacist to dispense the equivalent of a fortnight duration of medication at a time. This approach enabled the community pharmacist to supply medication continuously for collection every fortnight.

Patients attended the community pharmacy thereafter. The community pharmacist dispensed the medication fortnightly intervals unless identified otherwise by the TB specialist nurse.

The service specification allowed the community pharmacist to increase the intensity of the service to individual patients to a daily supervised consumption service, known as DOTs, if necessary. This would be in agreement with the patient and the TB specialist nurse and only for exceptional cases experiencing difficulties with adherence to medication but were motivated to continue treatment.

The intention was that all patients identified through screening requiring medication would access the new community pharmacy service to receive treatment. Upon review it was found that some patients accessed the Community Pharmacy Tuberculosis Medicines Compliance Scheme for treatment whilst others the usual hospital TB service. Patients were not randomised to one or the other service. The way patients accessed the services arose by chance.

## **5 Aims and objectives**

### **5.1 Aim**

**To evaluate a new community pharmacy service provided to improve adherence to medication for people identified with latent TB in upper Cwm Taf following a screening initiative.**

### **5.2 Objectives**

- To undertake a literature review to determine the evidence base for community pharmacy medication adherence interventions.
- To describe the characteristics of all patients diagnosed with latent TB following screening.
- To describe the patient pathways offered to those patients identified with latent TB following screening.
- To evaluate the community pharmacy service using Maxwell's dimensions of quality framework of effectiveness, efficiency, accessibility and acceptability (Maxwell 1984).

## **6 Method**

### **6.1 Literature review**

A literature review was undertaken to determine the evidence base for community pharmacy medication adherence interventions. The search strategy and results of the literature review are detailed in Appendix 2.

### **6.2 Data collection**

#### **6.2.1 Quantitative and patient specific data**

Data for all patients identified with latent TB and eligible for treatment were collected to inform the evaluation regardless of whether they fitted the exclusion criteria or not. Lists were prepared in an excel spreadsheet and each patient was given an identification number.

At screening, a consent form (to enable Mantoux testing to be performed on each patient), which also collected personal information, was completed for each patient. Consent forms were reviewed and data on age, gender and place of residence were collected for all patients.

Data were collected prospectively from the community pharmacy by completion of an audit and monitoring form. Audit, monitoring and return of data to Public Health Wales was built into the community pharmacy service specification from the outset.

A retrospective audit of patient medical records held at the hospital was undertaken to collect data regarding patients that accessed the routine hospital TB service and specialised hospital services.

Patient characteristics, which service was accessed and clinical information (whether treatment was reported as completed) was collected for all patients.

### **6.2.2 Data on costs**

Data of direct costs of the resources to provide both the community pharmacy service and the hospital service was identified. No indirect or intangible costs were collected.

Direct costs consisted of:

- service costs of the community pharmacy and hospital services including costs of professionals time;
- medicine costs, and
- cost of preparing and dispensing the medication.

As both groups of patients attended an assessment clinic, costs of the services accessed were calculated from the point of preparation of medication for supply at the relevant pharmacy.

Drug costs were calculated according to drug tariff prices for the community pharmacy service and hospital pharmacy drug acquisition costs.

The community pharmacy professional service fees were agreed at the outset in the service level agreement.

Hospital staff time was calculated and salary costs were provided by the finance department at the hospital. The time allocated by the hospital respiratory team for this work was calculated for each patient identified during the review of the patient medical record. A record was made of whether the individual attended the hospital or had received a home visit for a follow up appointment and time taken where the patient was contacted over the telephone. The overall time and associated costs were confirmed by the respiratory team. The hospital dispensing fees were identified from an All Wales hospital dispensing fee tariff in development.

### 6.2.3 Qualitative data

All patients (n=21) and stakeholders (n=8) were invited to participate in a semi-structured interview. Stakeholders were identified as either a commissioner or a provider of one of the services.

Interviews were conducted according to a protocol and prepared questions were used to guide the interview. Data from the interviews were collected by means of hand written notes and where possible audio taped and transcribed verbatim.

## 6.3 Ethics approval

Advice on whether ethical approval was required to conduct this evaluation was sought from the National Research Ethics Service. It was confirmed that ethical approval would not be required as this work was classed as service evaluation.

## 6.4 Evaluation framework

The community pharmacy service was evaluated against the usual care provided by the hospital. This would inform discussion not only as to whether the community pharmacist service was successful in providing treatment for patients with latent TB but also whether treatment outcomes were improved compared to usual care.

This evaluation used mixed methods and was based on a framework of Maxwell's dimensions of quality of effectiveness, efficiency, accessibility and acceptability.<sup>14</sup>

## 6.5 Population under study

The intention to treat population comprised of all patients identified as having latent TB identified through the screening initiative and eligible for treatment according to NICE guidelines 2006<sup>13</sup> i.e. patients who:

- had a positive Mantoux test measuring  $\geq 6$  mm with no history of previous BCG vaccination or a positive Mantoux test measuring  $\geq 15$  mm if they had had a BCG vaccination in the past;
- had a normal chest X ray, and
- were aged 2-34 years.

## 6.6 Exclusion criteria

This evaluation focuses on adult patients with latent TB who would normally access usual care at the hospital. The following groups of patients were therefore excluded:

- children under the age of 16 years;
- patients categorised as special cases due to unusual clinical conditions requiring specialist treatment;
- patients not presenting for treatment.

## 7 Key findings

### 7.1 Literature review

This literature search identified 1154 articles of which 10 relevant published articles were critically appraised. These consisted of:

- five randomised control trials (RCTs) covered in six articles<sup>15,16,17,18,19,20</sup> (one study was reported in two articles),
- two surveys<sup>21,22</sup> and
- two literature reviews.<sup>23,24</sup>

A summary of the critique of each article is presented in table format in Appendix 3.

Generally there appeared to be limited published evidence describing studies undertaken in the UK and assessing the role of the community pharmacists in adherence services. No study was reported on the role of a community pharmacist in providing medicine management services to patients with latent TB in the UK. This concurs with the findings of the Haynes et al. (2008) and Clifford et al. (2010) literature reviews.<sup>23,24</sup>

The results of a small number of RCTs and observational studies, conducted for differing clinical conditions, provide inconsistent evidence for the role of a community pharmacist in improving patient's adherence to medicines. The effectiveness of the community pharmacist intervention was reported to be non-significant in two RCTs and significant in three RCTs and one survey.

Studies were predominantly concerned with elderly patients, patients with chronic conditions or patients on multiple medications who tended to be older. Age in this instance could be a confounder for non-adherence and needs to be considered when drawing conclusions of community pharmacist interventions to a younger population (as in this evaluation) and the published literature.

No study looked at community pharmacist interventions compared to another service or intervention by a different healthcare professional. Benefits claimed could therefore be due to a healthcare professional intervention and not due to a community pharmacist intervention alone.

Sample sizes were small, and even in the larger studies, drop-out was considerable rendering the more robust trials under powered.

Without exception every study had potential for bias and confounding which could overestimate the benefits and effectiveness of the community pharmacist interventions reported. It was not possible to blind patients under study and thereby conceal which patients were receiving the intervention and which were not.

The duration of the studies varied from one week to 18 months but generally all studies were short when considering the majority of studies were in patients with long term conditions. Studies of such short periods provide a snapshot but not

necessarily sufficient evidence of non-adherence to long term treatment and the effect on clinical outcome. No study attempted to assess the long term effects of non-adherence on clinical outcome. Few studies measured clinical endpoints. Whether a change in adherence to medication is clinically important and has any long term effects on clinical outcomes was not tested or proven.

Few studies reported on cost effectiveness. Those that did reported varied results. Where the community pharmacist intervention was reported to be cost effective there was little proven benefit in patient outcomes.

This literature review provided an insight into the contribution community pharmacists can have on medication adherence. It strengthens the argument for studies, such as this evaluation, to be undertaken and published on the subject.

## **7.2 Patients identified with TB through screening**

A total of 332 people were screened for TB of which 132 people (53% of the 250 invitees) were invited by letter to attend and 200 people self presented at the screening events.

As a result, 21 patients, (n=15 of the invitees and n=6 of the self presenters), were found to have latent TB and be eligible for treatment. No patients were found to have active TB.

## **7.3 Patients included in the evaluation**

Of the 21 patients identified as eligible for treatment for latent TB, 13 patients were included in the evaluation and eight patients were excluded (Appendix 4)

Exclusions were:

- patients not presenting for treatment (n=3);
- children (n=3);
- patients managed by specialised clinic at hospital for another medical condition requiring treatment monitoring (n=1), and
- patients developing medical conditions during treatment resulting in treatment suspension or termination (n=1).

## **7.4 Demography**

### **7.4.1 Age**

The upper age limit of 35 was set according to guidance recommending that only patients under 35 years of age should be treated for latent TB.<sup>13</sup>

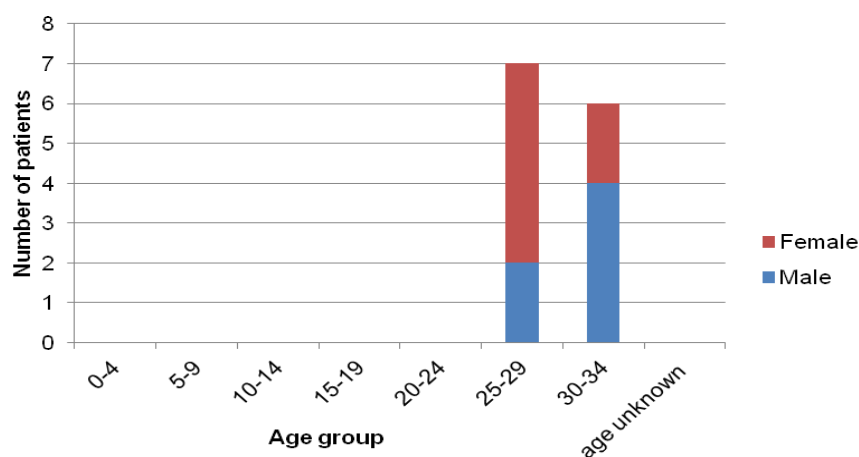
When exclusions were applied the 13 patients were concentrated in the 25-29 year and 30-34 year age groups (Table 1).

**Table 1: Breakdown of gender (by age group) of patients included in the evaluation**

| Broad age group<br>in years | Number of patients<br>Included in the evaluation |      |        |
|-----------------------------|--------------------------------------------------|------|--------|
|                             | Total                                            | Male | Female |
| <b>Number of patients</b>   | 13                                               | 6    | 7      |
| <b>25-29</b>                | 7                                                | 2    | 5      |
| <b>30-34</b>                | 6                                                | 4    | 2      |

#### 7.4.2 Gender

When exclusions were applied, of the 13 patients, there was approximately the same number of males and females (six male and seven female).

**Figure 3: Graph illustrating gender by age group of patients included in the evaluation**

More males (62.5%, n=5) accessed the community pharmacy service compared to the hospital service (20%, n=1) (Table 5).

**Table 2: Breakdown of gender (by age group) of patients accessing services**

| Broad age group<br>in years | Community pharmacy<br>service |      |        | Respiratory team at the<br>hospital service |      |        |
|-----------------------------|-------------------------------|------|--------|---------------------------------------------|------|--------|
|                             | Total                         | Male | Female | Total                                       | Male | Female |
| <b>25-29</b>                | 3                             | 1    | 2      | 4                                           | 1    | 3      |
| <b>30-34</b>                | 5                             | 4    | 1      | 1                                           | 0    | 1      |
| <b>Total persons</b>        | 8                             | 5    | 3      | 5                                           | 1    | 4      |

### 7.4.3 Place of residence

Nine of the 13 patients lived in the village. Of those one accessed the community pharmacy service regardless of their place of residence and three the hospital service.

**Table 3: Breakdown of place of residence for patients accessing the two services in the evaluation**

| Service accessed                         | Place of residence |                 |                     |
|------------------------------------------|--------------------|-----------------|---------------------|
|                                          | Total              | Local residents | Non-local residents |
| Community pharmacy service               | 8                  | 7               | 1                   |
| Respiratory team at the hospital service | 5                  | 2               | 3                   |

## 7.5 Effectiveness

Effectiveness was measured by whether the patient completed treatment or not.

### 7.5.1 Completion rates

Table 4 illustrates the proportion of patients that accessed the community pharmacy and the routine hospital service, the number completing treatment and the completion rate for the two services.

**Table 4: Breakdown of the number and treatment completion of patients accessing the community pharmacy and the routine hospital service**

| Medicine supplied by          | Did the patient complete the course of medicine |                                | Total |                 |                          |
|-------------------------------|-------------------------------------------------|--------------------------------|-------|-----------------|--------------------------|
|                               | Treatment completion unconfirmed                | Treatment completion confirmed |       | Completion rate | 95% Confidence intervals |
| <b>The community pharmacy</b> | 2<br>(25%)                                      | 6<br>(75%)                     | 8     | 0.75            | 0.41 - 0.93              |
| <b>The hospital service</b>   | 4<br>(80%)                                      | 1<br>(20%)                     | 5     | 0.2             | 0.04 - 0.62              |

Table 4 illustrates that six of the eight patients using the community pharmacy service and included in the evaluation completed treatment compared with one of the five patients using the usual hospital service and included in the evaluation.

Although the sample size of patients included in the evaluation is small, a difference in the proportion of patients completing treatment via the community pharmacy service compared to those that accessed the hospital service is observed.

The completion rate is observed to be greater in the group that accessed the community pharmacy.

### 7.5.2 Rate ratio

A rate ratio of the two services was calculated to be 3.75 (Table 5).

**Table 5: Rate ratio of the completion rates**

| Community pharmacy |                                                                                 | Hospital |                                                                               |
|--------------------|---------------------------------------------------------------------------------|----------|-------------------------------------------------------------------------------|
| Rate ratio         | = $\frac{\text{No. of observed successes}}{\text{Total No. using the service}}$ | /        | $\frac{\text{No. of observed successes}}{\text{Total No. using the service}}$ |
| Rate ratio         | = 0.75                                                                          | /        | 0.2                                                                           |
| Rate ratio         | =                                                                               |          | <b>3.75</b> (95% CI 0.621 – 22.644)                                           |

This suggest a possible 3.75 fold (CI 0.621 – 22.644) difference in effect with the community pharmacy service being at least three times more effective in supporting patients in completing their medication compared to the hospital service. However the small numbers involved mean that confidence intervals are wide, and statistical significance is not achieved.

### 7.5.3 Statistical analysis

Statistical analysis indicated difference in completion rates between community pharmacy service and the hospital service to be non-significant the p=0.103 (2 sided Fishers Exact test).

This does not necessarily support what we have observed in practice and what is considered clinically important. It should be noted that the numbers treated were small and a modest change in sample numbers may make the difference statistically significant.

## 7.6 Efficiency

### 7.6.1 Overall costs

A summary of the costs and is illustrated in Table 6.

A breakdown of detailed costs associated with each service is provided in Appendix 5.

**Table 6: Summary of direct costs used for cost effectiveness analysis**

| Resources                               | Costs in £                 |                  | Total           |
|-----------------------------------------|----------------------------|------------------|-----------------|
|                                         | Community Pharmacy service | Hospital service |                 |
| Total cost of service                   | £546.76                    | £490.05          | <b>£1036.81</b> |
| Number of patients                      | 8                          | 5                | 13              |
| Average cost per patient                | £68.35                     | £98.01           | NA              |
| Number of patients completing treatment | 6                          | 1                | 7               |
| <b>Cost per treatment completed</b>     | <b>£91.13</b>              | <b>£490.05</b>   | <b>-</b>        |

### 7.6.2 Cost effectiveness analysis

The overall cost of the hospital service at £490.05 was less costly than that of the community pharmacy at £546.76 (Table 6). However, the number of patients accessing each service differed creating a differential in the average cost per patient of £29.66. The average cost per patient of the hospital service being greater at £98.01 compared with the community pharmacy service at £68.35 (Table 6).

The cost per treatment completed was calculated to be £91.13 for the community pharmacy services compared with £490.05 for the hospital service (Table 6).

The cost per treatment completed as the unit of measure of cost effectiveness indicates that the community pharmacy service was less costly than the hospital service.

In summary the community pharmacy service was found to be the most cost effective service.

## 7.7 Accessibility and acceptability

All 21 patients were invited for interview of which seven respondents agreed initially to be interviewed and four patients were eventually attended for interview (response rate 19%). Each interview lasted approximately 45 minutes and was conducted either face to face or over the telephone.

The respondents had either accessed the community pharmacy or the hospital service as illustrated in Table 7.

**Table 7: Breakdown of patients interviewed**

| Patient identification | Service accessed   | Treatment completion Status |
|------------------------|--------------------|-----------------------------|
| R1                     | Community pharmacy | Confirmed completion        |
| R2                     | Hospital           | Confirmed completion        |
| R3                     | Community pharmacy | Confirmed completion        |
| R4                     | Hospital           | Unconfirmed completion      |

In general patient respondents were more concerned about the positive aspects of the screening events, specific issues with their medication and lack of information regarding follow up from the hospital rather than the quality of services provided. This is covered in part in the other themes section 7.8 of this report.

A total of 8 stakeholders agreed to be interviewed (response rate 100%) (Table 8).

Each interview lasted between 45 minutes to one hour and was conducted face to face at their place of work.

**Table 8: Breakdown of stakeholders interviewed**

| Stakeholder title                                     | Stakeholder status |
|-------------------------------------------------------|--------------------|
| Community pharmacist providing the new service        | Provider           |
| TB specialist nurse                                   | Provider           |
| Consultant Respiratory physician                      | Provider           |
| Consultant in communicable disease control            | Partner provider   |
| Local GP partner                                      | Provider           |
| Community Pharmacy Facilitator                        | Commissioner       |
| Chief pharmacist – Medicines management practice unit | Commissioner       |
| Director of Public Health ( Health Board)             | Commissioner       |

### 7.7.1 Accessibility

#### 7.7.1.1 Patient opinions on accessibility

Access was dealt with in the context of supply of medicine or access to professional advice and support for their treatment.

All four respondents expressed that they were happy with access for the supply of medication and access to professional advice when needed in their individual circumstances irrespective of the service accessed.

When asked where they would have preferred to have collected their medicines, three respondents indicated that the local community pharmacy was the preferred choice whilst one recognised the community pharmacy to be a suitable place to receive their medication.

When asked what was not so good about access to the TB services respondents had no negative issues to report which by omission suggests they were happy with the access.

One respondent expressed concern over the time between diagnosis and treatment.

When asked whether anything could have been done to make it easier to collect the TB treatment or get advice, respondents, in particular those who used the

community pharmacy, were complimentary about the service and could suggest no improvements.

#### **7.7.1.2 Stakeholder responses on accessibility**

All stakeholders believed that the new community pharmacy service would improve access for medication supply.

The majority of stakeholders were content for patients to access the community pharmacy for professional advice and support for their treatment.

- Only one respondent indicated that they would have preferred the usual care provided by the hospital.

Contact with the hospital service was minimal indicating the community pharmacist managed queries and provided adequate professional advice.

When asked *'How frequently do you think patients should collect their TB medication and have contact with a healthcare professional during their treatment?'* there was a difference in opinions.

- Four respondents felt that patients should collect their medication and have contact with a healthcare professional more frequently than that offered by the routine hospital service.
- Four respondents indicated that frequency of supply of medication and contact with a healthcare professional should be tailored for each patient.

When asked *'On a scale of 1-10 how effective do you think the Community Pharmacy Tuberculosis Medication Compliance Scheme was in improving access?'*

- Five respondents provided a score of 7 or greater
- Two respondents reported that they were unsure as they didn't know the results of the evaluation.
- One respondent did not provide a score but suggested access was improved.

When asked which service stakeholders thought patients would prefer:

- Five respondents suggested a service requiring frequent contact through the community pharmacy.
- Three respondents suggested services should be tailored to individual's circumstances.

## **7.7.2 Acceptability**

### **7.7.2.1 Patient opinions on acceptability**

The two respondents accessing the community pharmacy service expressed that they found the service acceptable.

When asked whether two weekly (fortnightly) collections of medicines from the pharmacy were acceptable or whether they would have preferred an alternative both respondents indicated they were happy with supplies every fortnight.

The two respondents who accessed the hospital service indicated they would have found the community pharmacy and acceptable option.

### **7.7.2.2 Stakeholder opinions on acceptability**

Acceptability was dealt with in the context of assumed acceptability for the patient or acceptability by the stakeholder.

- Five respondents indicated that they thought patients would find using the community pharmacy service acceptable whilst three respondents indicated they would not know how patients would perceive the community pharmacy service.
- Most stakeholders found using the community pharmacy as a new service provider acceptable to themselves.
- One stakeholder indicated they were not completely content with the new community pharmacy service.

When asking providers whether it had an impact on usual business responses varied.

- Six respondents including the community pharmacist indicated usual business was not adversely affected.
- Two respondents indicated their usual business was affected.

All respondents indicated that where they found the community pharmacy service acceptable, they expected the community pharmacy to at least have the facility of a private area (n=7) or a consultation area (n=1). In this case, the community pharmacy providing the service did not have a separate consultation area but a quiet area within the dispensary was available for private consultations.

## **7.8 Other themes identified during interview**

A number of key themes emerged during the interviews of both the patients and the stakeholders.

Patients identified concerns over the following issues:

- Problems with medication in particular the size of the tablets and adverse effects experienced.
- There was no alternative medication offered to patients who became non-adhered to treatment.
- Generally there appeared to be no choice as to which service the patients accessed. Only one patient suggested they were offered a choice of which service to access.
- All patients were uninformed about service provision post treatment. Two patients in particular were expecting a timely follow up by the hospital service. No patients had received contact from any service post treatment.

Stakeholders particularly identified concerns over the following:

- Communication between providers could have been better. This tended to be due to the process of communication methods used.
- There was an expectation by all except the community pharmacist that the community pharmacist would require training to provide the new service.
- Remuneration to the community pharmacist would require review if this service model was repeated as the workload was greater for the community pharmacist than anticipated for the remuneration agreed.

## 8 Discussion

This evaluation highlights the difficulties in ensuring people adhere to prescribed medication. It demonstrates that for a small group of selected patients with a specific disease a community pharmacist can provide a service which supports adherence to treatment.

Adherence is hard to quantify. Various measures for adherence have been reported in published studies such as self reported adherence and pharmacy refill counts. Such measures do not confirm whether the patient is actually taking the medicine and are subjective to responder bias potentially overestimating the adherence rates reported. Studies reporting on medication adherence are possibly overestimating the true extend of the medication adherence.

In this pilot the community pharmacist took the initiative to request that the patient return their empty medication foils as a marker to detect non-adherence. This was used together with pharmacy collection records and adhoc self reporting of adherence to measure adherence and treatment completion.

Overall across both the community pharmacy and the hospital service six of the 13 patients did not adhere to treatment and failed to complete the course of medication. Potentially these individuals remain at risk of developing active TB and spreading the disease.

The literature review found no UK published studies assessing community pharmacist interventions to support adherence to latent TB treatment. Some studies (non-UK) conducted in settings other than a community pharmacy report adherence rates and therefore completion for latent TB treatment to be between 48% and 65% for nine months therapy of isoniazid as a single therapy<sup>25,26,27,28,29</sup> and between 72% to 85% for four months therapy of rifampicin as a single therapy.<sup>25,28,29</sup> An unpublished audit of one of the busiest hospital TB service in Wales reported treatment completion rates of 61% for chemoprophylaxis (using isoniazid alone or combined rifampicin and isoniazid).<sup>30</sup>

This evaluation reported completion rates of 20% for the hospital service and 75% for the community pharmacy service. This suggests that the completion rate for the hospital service was lower than reported by other hospital led TB services in Wales. As data on completion rates for latent TB treatment is not routinely collected, it is unknown whether the 20% completion rate reported for the hospital service is lower than expected or standard for that service.

The community pharmacy service was observed to be more effective in supporting adherence to treatment for latent TB than the hospital service but this was not statistically significant. It is however clinically important as a higher proportion of patients completed treatment via the community pharmacy than usual care. For these patients the risk of developing active TB was minimised and the spread to the wider local population reduced. If the effectiveness observed was on a larger scale with a greater sample size, the clinical importance increases.

The community pharmacy service was found to be more cost effective than the hospital service. A review of remuneration as suggested following interviews would may affect the cost of the community pharmacy service but the differential between the costs of the two services would suggest that community pharmacy service would remain the more cost effective service. This is important in informing decisions on healthcare spend and value for money of healthcare services.

Both patients and stakeholders reported the community pharmacy service accessible and acceptable.

## 8.1 Limitations

### 8.1.1 Sample size

A sample size calculation indicated the study was underpowered to detect significance. A suggested sample of 120 patients (60 accessing the community pharmacy and 60 the hospital care) would be required to detect a two-fold difference of effect in favour of the community pharmacy service. This is based on an alpha of 0.05 (two sided) and a power of 80%.

This is feasible as approximately 180 patients are identified with active TB annually in Wales of which at least 180 contacts will be treated for latent TB. It would not be difficult to identify 120 patients with latent TB to provide the sample required and design a study randomising patients identified with latent TB to a service provided by either a community pharmacist or the hospital service. The results could be collected

and a meta-analysis performed to detect statistically whether using a community pharmacy service does improve adherence.

Due to low incidence of TB in Wales and the circumstances of the screening initiative, it was not possible to increase the sample size ( $n=13$ ) for this situation to increase the power of the study.

### **8.1.2 Chance**

It is possible that the results of the effectiveness observed have arisen by chance due to the small sample size available.

Due to the small sample size it is possible that the result of the statistical analysis is a Type II error and there really was a statistically significant difference in completion rates between the two services.

### **8.1.3 Bias affecting effectiveness**

The evaluation revealed that the hospital service records, on occasion, were incomplete and it is possible that assumptions were made regarding the unconfirmed treatment completion of patients accessing the hospital service. Where possible, confirmation of treatment completion was made verbally with the TB specialist nurse and contact with patients in arranging interviews. Data were analysed according to the information available. This could introduce a potential recording bias and underestimate the effectiveness of the hospital service.

It is possible that there was a difference in the two groups under evaluation. The group of patients accessing the community pharmacy service attended the community assessment clinic and thereby potentially showed a greater level of motivation to access services and complete treatment. The converse could also be argued that patients who accessed the hospital service as a result of not attending the community assessment clinic or making contact at a later date were the more motivated group as they had taken the initiative to contact the service and attend the hospital, some distance away, for assessment before commencing treatment.

### **8.1.4 Bias affecting efficiency**

Direct costs were used for the cost effectiveness analysis. Indirect costs such as lighting, heating, accommodation cost were not included which potentially could affect either or both service costs.

No costs were included for training the community pharmacist. In this case the community pharmacist was adequately informed due to history of TB in the area. The stakeholder interviews suggested that training for the community pharmacist may be required if the service was repeated using a different pharmacist. This could potentially increase the cost of the community pharmacy service if repeated.

Remuneration for the community pharmacy service was agreed the outset. Interviewees suggested that remuneration would require review as the workload was greater than anticipated if the service was repeated. As the differential of cost per treatment completed between the two services is so great it is unlikely that an uplift in service costs would render the community pharmacy service less cost effective than the hospital service. However this would need to be explored further.

Travel costs incurred by the TB specialist nurse as a result of house visits was not made available for this evaluation and was not included in the CEA. Although potentially a small value eliminating this cost from the results would underestimate the true cost per treatment completion of the hospital service.

#### **8.1.5 Bias affecting accessibility and acceptability**

Interviews took place approximately 9 months after the patients were treated and the services were operated. Recall bias would inevitably affect the accounts of both the patient and stakeholders being interviewed. This is reflected in the interviews where on occasion “do not know” or “can’t remember” was reported. It did not however detract from providing sufficient evidence to report that for the majority of respondents the community pharmacist service was reported as accessible and acceptable.

#### **8.1.6 Generalisability of the community pharmacy service**

This service was provided by a single community pharmacist who was particularly motivated and engaged from the outset. This was demonstrated by attendance at meetings held during the planning stages and attendance at screening events. The enthusiasm of the community pharmacist was noted by both stakeholders and patients during interviews. The pharmacist had an established presence and had a trusted relationship with the majority of patients under evaluation, many of whom had used the pharmacy regularly for other purposes. This could have influenced the success observed in treatment completion of the group of patients which accessed the community pharmacy and affect the generalisability of the results.

### **8.2 Lessons learned**

A number of issues were identified during the evaluation:

- Data on latent TB is not collected centrally and is reliant on local services for monitoring purposes. As a result there is no standardised dataset making it difficult to collate information to monitor latent TB on a Wales wide scale and make comparisons between services.
- Data held at the hospital was incomplete and on occasion inadequate for evaluation purposes. This was because there was no obligation for the hospital to routinely collect information for evaluation. An assumption was made at the outset that data collected for the hospital service would be

adequate for monitoring and evaluation purposes. If repeated, criteria for audit and monitoring for all services should be prepared in advance of implementation.

- Data collected by the pharmacist operating the Community Pharmacy Tuberculosis Medicines Compliance Scheme was complete and appropriate for use for evaluation. This was because audit and monitoring was designed to be a crucial element of the community pharmacy service. This should be replicated across all services if repeated.
- Getting patients to agree to be interviewed was a challenge. Interviews were conducted months after their treatment had finished. For some patients contact phone numbers and address had changed. This is a common problem in deprived communities where people in social housing move frequently, do not have landline telephones and rely on mobile phone use where contracts and phone numbers often change.
- It was underestimated how difficult some patients would find taking the TB medication. This was either because of the size of the tablets or the adverse effects experienced. No alternative form, e.g. liquid, or drug choice were considered or offered when patients raised issues which may affect adherence. This may have contributed towards some patients not completing treatment.

## 9 Conclusion

The community pharmacy service appears more effective, although this was not statistically significant, and was more cost effective than the hospital service. It was accessible and acceptable to patients and stakeholders.

This model should be considered when providing future treatment to patients for latent TB. The community pharmacy services described in this evaluation could be replicated for use with other medical conditions where medication adherence is clinically important and known to be poor.

## 10 References

1. Stevenson F. Concordance: what is the relevance for pharmacists? *Int J Pharm Pract* 2001; 9: 67-70.
2. National Institute for Health and Clinical Excellence. *Medicines adherence. Involving patients in decisions about prescribed medicines and supporting adherence*. CG76. London: NICE; 2009. Available at: <http://guidance.nice.org.uk/CG76/NICEGuidance/pdf/English> [Accessed 10<sup>th</sup> Feb 2011].
3. Pruce D. Minimising patient non-adherence in practice. *Pharm J* 2011; 286: 45.
4. Pruce D. Detecting poor adherence in practice. *Pharm J* 2011; 286: 114.
5. Health Protection Agency. 2011. *Tuberculosis (TB)*. [Online]. Available at: <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Tuberculosis/> [Accessed 1<sup>st</sup> Nov 2011].
6. Centres for Disease Control and Prevention. 2011. *Tuberculosis (TB) fact sheet*. [Online]. Available at: <http://www.cdc.gov/tb/publications/factsheets/general/LTBlandActiveTB.htm> [Accessed 3<sup>rd</sup> Nov 2011].
7. World Health Organisation. 2011. *Tuberculosis*. Fact sheet N°104. [Online]. Available at: <http://www.who.int/mediacentre/factsheets/fs104/en/> [Accessed 1<sup>st</sup> Nov 2011].
8. Public Health Wales. 2011. *Tuberculosis*. [Online]. Available at: <http://www.wales.nhs.uk/sites3/page.cfm?orgId=457&pid=27952> [Accessed 10<sup>th</sup> Feb 2011].
9. National Public Health Service for Wales. *Enhanced TB surveillance, Annual report for Wales. Data to the end of 2009*. Cardiff: NPHS; 2009. Available at: [http://www2.nphs.wales.nhs.uk:8080/CommunitySurveillanceDocs.nsf/3dc04669c9e1eaa880257062003b246b/98e7f91c7f51907c802577f20056304b/\\$FILE/20100212\\_AnnualE\\_TSRpt\\_RH\\_1.doc](http://www2.nphs.wales.nhs.uk:8080/CommunitySurveillanceDocs.nsf/3dc04669c9e1eaa880257062003b246b/98e7f91c7f51907c802577f20056304b/$FILE/20100212_AnnualE_TSRpt_RH_1.doc) [Accessed 10<sup>th</sup> February 2011].
10. British National Formulary. *Infections. Antituberculosis drugs*. BNF 2010; 59: 348-52.
11. National Institute for Health and Clinical Excellence. *Tuberculosis. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control*. CG117. London: NICE; 2011. Available at: <http://guidance.nice.org.uk/CG117/Guidance/pdf/English> [Accessed 10<sup>th</sup> Feb 2011].
12. Public Health Wales. 2010. *Successful first week for TB community screening sessions*. [Online]. Available at: <http://www.wales.nhs.uk/sitesplus/888/news/15991> [Accessed 14<sup>th</sup> Feb 2011].
13. National Institute for Health and Clinical Excellence. *Tuberculosis. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control*. CG33. London: NICE 2006. Available at: <http://guidance.nice.org.uk/CG33/NICEGuidance/pdf/English> [Accessed 10<sup>th</sup> Feb 2011].

14. Maxwell RJ. Quality assessment in health. *Br Med J* 1984; 288: 1470-1.
15. Blenkinsopp A et al. Extended adherence support by community pharmacists for patients with hypertension: a randomised controlled trial. *Int J Pharm Pract* 2000; 8: 165-75.
16. Sturgess I et al. Community pharmacy based provision of pharmaceutical care to older patients. *Pharm World Sci* 2003; 25: 218-26.
17. Clifford S et al. Patient centred advice is effective in improving adherence to medicines. *Pharm World Sci* 2006; 28:165-70.
18. The Community Pharmacy Medicines Management Project Evaluation Team. The MEDMAN study. A randomized controlled trial of community pharmacy-led medicines management for patients with coronary heart disease. *Fam Pract* 2007; 24: 189-200.
19. Elliott RA et al. Cost-effectiveness of a telephone based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharm World Sci* 2008; 30: 17-23.
20. Desborough JA et al. Medicines use reviews (MURs): what is their effect on adherence and satisfaction? A pilot study. *Int J Pharm Pract* 2008; 3: C16.
21. Barber N et al. Patients' problems with new medication for chronic conditions. *Qual Saf Health Care* 2004;13:172-5.
22. Raynor AK et al. The development and evaluation of an extended support programme by community pharmacists for elderly patients at home. *Int J Pharm Pract* 2000; 8: 157-64.
23. Haynes RB et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. Issue 4. 2008; Art. No.: (2):CD000011. Available at: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000011.pub3/pdf> [Accessed 15<sup>th</sup> Feb 2011].
24. Clifford S et al. Medication adherence and community pharmacy: a review of education, policy and research in England. *Pharmacy Practice* 2010; 8: 77-88.
25. Cook PP et al. Safety and completion rate of short-course therapy for treatment of latent tuberculosis infection. *Clin Infect Dis* 2006; 43: 271- 5.
26. Horsburgh CR Jr. et al. Latent TB infection treatment acceptance and completion in the United States and Canada. *Chest* 2010; 137: 401-9.
27. Kwara A et al. Factors associated with failure to complete isoniazid treatment for latent tuberculosis infection in Rhode Island. *Chest* 2008; 133: 862-8.
28. Lardizabal A et al. Enhancement of treatment completion for latent tuberculosis infection with 4 months of rifampicin. *Chest* 2006; 130: 1712-7.
29. Li J et al. Adherence to treatment of latent tuberculosis infection in a clinical population in New York City. *Int J Infect Dis* 2010; 14: 292-7.

30. Martin C. *An audit of adherence to chemoprophylaxis of latent TB in Cardiff and Vale NHS Trust in 2007*. 5th Year Senior Project. Cardiff University School of Medicine. [unpublished]
31. Andrade ASA et al. A programmable prompting device improves adherence to highly active antiretroviral therapy in HIV-infected subjects with memory impairment. *Clin Infect Dis* 2005; 41: 875-82.
32. Beaucage K et al. Telephone follow-up of patients receiving antibiotic prescriptions from community pharmacies. *Am J Health-Syst Pharm* 2006; 63: 557-63.
33. Lee JK et al. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low density lipoprotein cholesterol: a randomized controlled trial. *JAMA* 2006; 296: 2563-71.
34. Nazareth I et al. A pharmacy discharge plan for hospitalised elderly patients-a randomised controlled trial. *Age Aging* 2001; 30: 33-40.
35. Odegard PS et al. Caring for poorly controlled diabetes mellitus: a randomized pharmacist intervention. *Ann Pharmacother* 2005; 39: 433-40.
36. Peterson GM et al. Impact of pharmacist-conducted home visits on the outcomes of lipid-lowering drug therapy. *J Clin Pharm Ther* 2004; 29: 23-30.
37. Rickles NM et al. Pharmacist telemonitoring of antidepressant use: effects on pharmacist-patient collaboration. *J Am Pharm Assoc* 2005; 45: 344-53.
38. Sadik A et al. Pharmaceutical care of patients with heart failure. *Br J Clin Pharmacol* 2005; 60: 183-93.
39. Stevens V et al. Helicobacter pylori eradication in dyspeptic primary care patients: a randomized controlled trial of a pharmacy intervention. *West J Med* 2002; 176: 92-6.
40. Volume CI et al. Pharmaceutical care research and education project: patient outcomes. *J Am Pharm Assoc* 2001; 41: 411-20.
41. Weinberger M et al. Effectiveness of pharmacist care for patients with reactive airways disease: a randomized controlled trial. *JAMA* 2002; 288: 1594-1602.
42. Solutions for Public Health. 2010. *Critical appraisal skills programme*. [Online]. Available at: <http://www.sph.nhs.uk/what-we-do/public-health-workforce/resources/critical-appraisals-skills-programme> [Accessed 3<sup>rd</sup> May 2011].

**Appendix 1*****Community Pharmacy Tuberculosis Medicines Compliance Scheme******Local Enhanced Service*****PART A - SERVICE SPECIFICATION****1. SERVICE DESCRIPTION**

1.1 The named pharmacist(s) shall provide advice, support and assistance to the person with a view to improving the patient's knowledge and use of their drugs and their compliance.

1.2 The named pharmacist will provide a TB medicines compliance service consisting of dispensing TB medication against an individual care plan prepared by the TB specialist nurse for each patient indicating measures to improve compliance this could be:

- contacting the TB specialist nurse when regular repeat prescriptions for TB medication is not collected for a period of two days
- provision of weekly / monthly medication administration charts if identified in the care plan
- provision of weekly dispensed TB medication in bottles if identified in the care plan
- provision of weekly dispensed monitored dosage systems if identified in the care plan
- provision of supervised administration (Direct Observed Therapy – DOTS) at intervals identified in the care plan, this may be daily or twice / three times weekly.

The named pharmacist will be expected to keep an ongoing monitoring system that will identify when an individual's prescription is due and contacting the TB specialist nurse when a period of 2 days has passed without the prescription being presented and / or dispensed.

**Appendix 1 continued****2. AIMS AND INTENDED SERVICE OUTCOMES**

2.1 The pharmacy will support patients, over and above the Dispensing Essential service, to ensure compliance of their TB by:

- ◆ improving the patient's understanding of their medicines;
- ◆ alerting the TB specialist nurse of individual's non – compliance;
- ◆ where possible, simplifying the medicines regimen and ordering process where appropriate;
- ◆ identifying practical problems in taking their medicines and where appropriate identifying the need for compliance aids,

**3. REIMBURSEMENT**

3.1 The fee payable for the provision of the *Tuberculosis Medicines Compliance Scheme* is a combination of a Monitoring and Audit Fee and a professional fee for each element of the service provided.

(a) Monitoring and Audit Fee £xxx (ARFs need

(b). Professional Fees

i. Provision of medication administration charts

ii. Provision of weekly bottle dispensed TB medication

iii. Provision of weekly monitor dosage systems

iv. Provision of supervised administration

3.2 Drug costs will be reimbursed at Drug Tariff prices.

3.3 The monitoring and audit fee will be paid annually at first provision of the service.

3.4 The monitoring and audit fee includes 60 minutes of overall service audit and feedback time per annum. Additional requirements will be reimbursed at the CPW agreed rates.

3.5 The Fees issued will be paid monthly in arrears.

3.6 The above fees will be paid from: **1<sup>st</sup> April 20-- to 31<sup>st</sup> March 20--**

3.7 Reimbursement rates for the service will be reviewed prior to January each year and the revised rates will be effective from the 1<sup>st</sup> April.

3.8 Claims for payment will be made using the Claim and Audit Form.

3.9 Claims for payment will be subject to the LHB's Post Payment Verification Process.

**Appendix 2****Literature review method and search strategy**

Articles were limited to the English language and humans.

The search was limited to the last 15 years (1996 - week 1 June 2011) to ensure studies identified were relevant to the current situation.

Medline, Embase and the Health Management Information Consortium (HMIC) were searched.

The search was expanded to include the following Cardiff University online journal databases; Pharmacy World and Science, the Pharmaceutical Journal, Family Practice, the online Cochrane library and Google and Google Scholar to identify grey literature.

Studies were included if they were undertaken with adults, undertaken in the UK, undertaken in a community pharmacy setting, reported adherence (to medication) and / or reported drug treatment completion.

Studies were excluded if they were undertaken with adults with HIV, undertaken with children only and undertaken outside UK.

The table below illustrates the keywords and combined terms used to search the electronic databases.

**Table illustrating keywords and combined terms used in the search**

| Subject heading                              | Keyword                                                                                                                                                                    |
|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Exp. Medication adherence<br>Exp. Pharmacies | Medication adherence<br>Medication compliance<br>Treatment completion<br>Treatment compliance<br>Community pharmacy<br>Community pharmacist<br>Community pharmacy services |

Identified papers were critically appraised using CASP framework<sup>37</sup>

Table 1: Randomised Controlled Trials (RCTs)

|              | Blenkinsopp A<br>et al 2000 <sup>15</sup>                                                                                                                                                                                               | Sturgess IK<br>et al 2003 <sup>16</sup>                                                                                                                                                                                                                                                            | Clifford S<br>et al 2006 <sup>17</sup>                                                                                                                                                                                                                                                      | MEDMAN 2007 <sup>18</sup>                                                                                                                                                                                                                                                                  | Elliott RA<br>et al 2008 <sup>19</sup>                           | Desborough J<br>et al 2008 <sup>20</sup>                                                                                                                  |
|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Study design | RCT                                                                                                                                                                                                                                     | RCT                                                                                                                                                                                                                                                                                                | RCT                                                                                                                                                                                                                                                                                         | RCT                                                                                                                                                                                                                                                                                        | RCT                                                              | RCT                                                                                                                                                       |
| Study length | 20 months                                                                                                                                                                                                                               | 18 months                                                                                                                                                                                                                                                                                          | 4 weeks                                                                                                                                                                                                                                                                                     | 12 months                                                                                                                                                                                                                                                                                  | as per Clifford<br>2006 study                                    | 1 week                                                                                                                                                    |
| Objective    | To determine effects of a patient centred intervention by community pharmacists on adherence to treatment for hypertension.                                                                                                             | To measure the outcomes of a pharmaceutical care programme by community pharmacists to elderly patients.                                                                                                                                                                                           | To assess the effects of pharmacists giving advice to meet patients' needs after starting a new medicine for a chronic condition.                                                                                                                                                           | To test whether a community pharmacy led service would improve a range of measures including compliance and be cost effective.                                                                                                                                                             | To assess the cost effectiveness of pharmacist telephone advice. | To provide estimates of the level of patient reported adherence and satisfaction following a Medicine Use Review (MUR) that could be used to power a RCT. |
| Intervention | Pharmacist delivered patient questionnaire (by telephone if necessary) on 3 occasions at 2 months intervals over a six month period.<br><br>Advice, information and referral to the patient's GP was undertaken according to responses. | Community pharmacists assessing individual patient's medicine related problems using study questionnaire.<br><br>Self completed and interview questionnaires (by a different staff member) used to collect data at 6, 12 and 18 months.<br><br>Intervention tailored to individual patients needs. | Semi structured telephone interviews by community pharmacist based in Moss head office – 2 weeks post recruitment.<br><br>Follow up telephone interview to intervention group by researcher and postal questionnaire to all patients at 4 weeks - 2 <sup>nd</sup> questionnaire at 8 weeks. | Face to face consultations with community pharmacist.<br><br>Patients recruited from 48 GP practice registers and invited to participate. 70 pharmacies given 20 patients to manage.<br><br>Baseline and follow up data collected from GP systems and patient self reported questionnaire. | as per Clifford 2006 study.                                      | Base line questionnaire and follow up postal questionnaire one week after medication usage review undertaken by pharmacist.                               |

Table 1: Randomised Controlled Trials (RCTs)

|                                   | Blenkinsopp A<br>et al 2000 <sup>15</sup>                                                                                                 | Sturgess IK<br>et al 2003 <sup>16</sup>                                                                         | Clifford S<br>et al 2006 <sup>17</sup>                                                                                  | MEDMAN 2007 <sup>18</sup>                                                                                                      | Elliott RA<br>et al 2008 <sup>19</sup>                                                      | Desborough J<br>et al 2008 <sup>20</sup>                                             |
|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| <b>Population characteristics</b> | 180 patients treated for hypertension drawn from 20 community pharmacy sites and 43 GP practices in one health authority area in England. | 191 patients 65 + years, taking 4 or more medicines, living at home from 10 community pharmacies in N. Ireland. | 500 patients 75 + years prescribed a new medicine for a chronic condition drawn from 40 Moss pharmacies across England. | 1493 patients over 17 years of age and with CHD registered with one of the 164 GP practices across nine sites in England.      | as per Clifford 2006 study.                                                                 | 72 patients drawn from 7 pharmacies – pharmacies identified by convenience sampling. |
| <b>Intervention group</b>         | 101 patients from 11 pharmacies                                                                                                           | 110 patients from 5 pharmacies                                                                                  | 255 patients                                                                                                            | 980                                                                                                                            | as per Clifford 2006 study                                                                  | Not reported.                                                                        |
| <b>Control Group</b>              | 79 patients from 9 pharmacies                                                                                                             | 81 patients from 5 pharmacies                                                                                   | 237 patients                                                                                                            | 513                                                                                                                            | as per Clifford 2006 study                                                                  | Not reported.                                                                        |
| <b>Power</b>                      | Not reported.                                                                                                                             | Not reported.                                                                                                   | Not reported but author recognises effect of large number of drop-outs underpowered study.                              | Sample size calculation undertaken for 90% power to detect a 6% change in patients receiving aspirin at 5% significance level. | Sample size calculation for 80% power to detect a 10% reduction in self reported adherence. | Not reported.                                                                        |
| <b>Randomisation</b>              | Sequentially at pharmacy level.                                                                                                           | At pharmacy level, recruited sites matched into pairs according to size, location and pharmacy then randomised. | At patient level done by the pharmacist (blinded to envelope content) recruiting patients by sealed envelope.           | At patient level intervention: control 2:1 by an independent researcher using computer programme.                              | as per Clifford 2006 study.                                                                 | Unexplained.                                                                         |
| <b>Adherence definition</b>       | No definition - scoring according to answers. Scores of 33/ 35 or less non-adherent.                                                      | No definition of adherence provided.                                                                            | Self report of at least one dose missed in the last 7 days.                                                             | No definition of adherence (compliance) provided.                                                                              | as per Clifford 2006 study.                                                                 | No definition but adherence score using validated scoring tool MARS.                 |

Table 1: Randomised Controlled Trials (RCTs)

|                                      | Blenkinsopp A<br>et al 2000 <sup>15</sup>                                                                                                                                                                                                                                                                                                                                                                                                 | Sturgess IK<br>et al 2003 <sup>16</sup>                                                                                                                                                                                                                                                                                                                                                                                                                            | Clifford S<br>et al 2006 <sup>17</sup>                                                                                                                  | MEDMAN 2007 <sup>18</sup>                                                                                                                                                                                                                                                           | Elliott RA<br>et al 2008 <sup>19</sup>                                                                                                                                                                                                                      | Desborough J<br>et al 2008 <sup>20</sup>                                                                                                            |
|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Adherence Measures</b>            | Self reported adherence (pre and post postal questionnaire) & pharmacy refill collection.                                                                                                                                                                                                                                                                                                                                                 | Compliance with dosage regimes.                                                                                                                                                                                                                                                                                                                                                                                                                                    | Incidence of non-adherence – self reported at 4 weeks.                                                                                                  | Compliance with treatment.                                                                                                                                                                                                                                                          | as per Clifford 2006 study.                                                                                                                                                                                                                                 | Self reported adherence measured using validated scale.                                                                                             |
| <b>Results of adherence measures</b> | <p>Adherence statistically significantly higher in the intervention group (62.9%) compared with control (50%) <math>p&lt;0.05</math>.</p> <p>Change from baseline adherence rates greater for intervention group (52.3% to 62.9%) compared to control (51% to 50%).</p> <p>30% patients still taking medication non-adherence at 10 days (n=67/227).</p> <p>17% patients still taking medication non-adherence at 4 weeks (n=29/171).</p> | <p>Statistically significant higher proportion of patients self reported compliant with medication at 12 months (40.4% v 24.4 % control) and 18 months (47.3% v 14.7% control) <math>p&lt;0.05</math>.</p> <p>Statistical differences between groups of self reported adherence at 6 months not reported but pharmacy refill records showed a statistically significant proportion of patients compliant in intervention v control groups <math>p=0.02</math>.</p> | <p>Non-adherence 9% (16/185) intervention group 16% (31/194) control <math>p=0.032</math> (of the patients still prescribed medication at 4 weeks).</p> | <p>The total score for patient compliance and median IQR was the same for both the intervention and the control group (59 (IQR 56-60)</p> <p>No statistical difference in self reported compliance between groups</p> <p>(similar at baseline) <math>p=0.99</math> (0.61-1.65).</p> | <p>Response rate to 4 week questionnaires 72% intervention 62% control.</p> <p>Non-adherence significantly lower in intervention group (10/87 11%) v control (23/118 19%) <math>p&lt;0.05</math> at 4 weeks</p> <p>(205 patients used in the analysis).</p> | <p>87% patients completed follow up questionnaire (n=63).</p> <p>Non-significant increase in mean adherence score of 0.15 (95% CI - 0.37-0.67).</p> |
| <b>Other measures</b>                | Control of blood pressure – measurement collected retrospectively from GP record.                                                                                                                                                                                                                                                                                                                                                         | Health related quality of life, number of hospitalisations, sign and symptoms control, patient knowledge of medicines, drug use,                                                                                                                                                                                                                                                                                                                                   | <p>Problems with new medicines.</p> <p>Beliefs about the new medicine.</p>                                                                              | Appropriate treatment according to the National Service Framework for CHD.                                                                                                                                                                                                          |                                                                                                                                                                                                                                                             | Satisfaction with information about medicines.                                                                                                      |

Table 1: Randomised Controlled Trials (RCTs)

|                                   | Blenkinsopp A<br>et al 2000 <sup>15</sup>                                                                                                                                                                                                                                                                                                                                   | Sturgess IK<br>et al 2003 <sup>16</sup>                                                                                                                                                                                                                                                              | Clifford S<br>et al 2006 <sup>17</sup>                                                                                                                                                                                                                                                | MEDMAN 2007 <sup>18</sup>                                                                                                                                                                                                       | Elliott RA<br>et al 2008 <sup>19</sup>                                                                                                                                                               | Desborough J<br>et al 2008 <sup>20</sup>                                                                                                                                                                                       |
|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                   | Satisfaction of pharmacy service by means of pre and post postal questionnaire.                                                                                                                                                                                                                                                                                             | changes of medicines, and contacts with health professionals.<br><br>Patient satisfaction.                                                                                                                                                                                                           | Safety and usefulness of intervention.                                                                                                                                                                                                                                                | Health status.<br><br>5 yr risk of CVD death.<br><br>Patient satisfaction.                                                                                                                                                      |                                                                                                                                                                                                      |                                                                                                                                                                                                                                |
| Economic measures                 |                                                                                                                                                                                                                                                                                                                                                                             | Difference in costs of medicines in intervention group v control approaching statistical significance p=0.06 at 6 months but no different at 12 or 18 months.                                                                                                                                        |                                                                                                                                                                                                                                                                                       | Cost minimisation analysis £970.50 per patient for intervention v £835.2 per patient for control at follow up. Costs high for pharmacy intervention due to training costs.                                                      | Intervention more effective and less costly (mean ICER - £2168 per adherent patient).                                                                                                                |                                                                                                                                                                                                                                |
| Confounding factors / limitations | Author recognises potential for bias in randomisation thereby overestimating intervention success<br><br>Pharmacy recruitment potentially introducing bias.<br><br>Difficulty in obtaining BP measurements retrospectively meant missing data – only 63 / 180 patients data complete.<br><br>Authors note that the number of patients in study was small but 'sufficient to | Large drop-out rate – 60% intervention and 40% controls completed study).<br><br>Intervention patients prescribed statistically significant greater number of medications at baseline p<0.05.<br><br>No definition of adherence.<br><br>Different interventions tailored to patients making analysis | Large drop-out - 47% (123/ 261) intervention group and 51% (124/239).<br><br>Author notes this as a limitation which left the study underpowered.<br><br>Generalisability to high street community pharmacy questionable as intervention carried out from head office although author | Patients could not be blinded because of design of intervention.<br><br>205 of initially 500 patients recruited used for analysis of adherence.<br><br>Adherence at 4 weeks was checked and assumed to be the same at 2 months. | Limitations cited by author - methods used to recruit pharmacies, adherence measure, length to follow up, loss to follow up<br><br>Patients not speaking English or not having a telephone excluded. | Overall small sample size (n=72), only 63 patients completing follow up questionnaire.<br><br>No sample size calculation to ensure power of study.<br><br>No explanation how patients chosen to intervention or control group. |

Table 1: Randomised Controlled Trials (RCTs)

|                 | Blenkinsopp A<br>et al 2000 <sup>15</sup>                                                                                                                                                                                                                                                                         | Sturgess IK<br>et al 2003 <sup>16</sup>                                                                                                                                                                                        | Clifford S<br>et al 2006 <sup>17</sup>                    | MEDMAN 2007 <sup>18</sup>                                                                                                                         | Elliott RA<br>et al 2008 <sup>19</sup>                                                                                             | Desborough J<br>et al 2008 <sup>20</sup>                                                                                                                                                                                                             |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                 | <p>allow statistical analysis' however no sample size calculation reported.</p> <p>Self reporting adherence pre and post intervention.</p> <p>No economic or cost effectiveness analysis included.</p>                                                                                                            | <p>difficult and results open to interpretation.</p> <p>Difficulties in recruitment of pharmacies and patients –motivated participated querying generalisability.</p>                                                          | <p>claims this 'could be delivered in practice'</p>       |                                                                                                                                                   | <p>No economic or cost effectiveness analysis included.</p>                                                                        | <p>Number and characteristics of intervention and control group not stated.</p> <p>No economic or cost effectiveness analysis included.</p>                                                                                                          |
| <b>Comments</b> | <p>First UK study to test the effect of community pharmacy intervention on adherence to treatment. Observed effect may be due to information tailored to patients or increased time with pharmacist empowering them to ask questions.</p> <p>Community pharmacists can produce positive effects of adherence.</p> | <p>Pharmaceutical care resulted in improvement in medication compliance but limited impact on healthy related quality of life, patient knowledge of medicines and healthcare utilisation.</p> <p>Further studies required.</p> | <p>Economic analysis and intervention cost effective.</p> | <p>Largest RCT in community pharmacy setting in UK.</p> <p>Difference in cost was statistically different due to cost of pharmacist training.</p> | <p>Evidence that a telephone call from a pharmacist can significantly reduce non-adherence and is less costly than usual care.</p> | <p>This was a pilot study with a small number of patients. Adherence scores were high at the start of the study limiting ability to show effect of MUR. Small differences in adherence believed to be clinically important. A larger RCT needed.</p> |

Table 2: Surveys and service evaluations

|                                   | Raynor DK<br>et al 2000 <sup>22</sup>                                                                                                                                                                                                                                                                       | Barber N<br>et al 2004 <sup>21</sup>                                                                                                                                                                                |
|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Study design</b>               | Survey (Before and after study)                                                                                                                                                                                                                                                                             | Survey                                                                                                                                                                                                              |
| <b>Study length</b>               | Not reported – potentially 2-6 months                                                                                                                                                                                                                                                                       | 12 months                                                                                                                                                                                                           |
| <b>Objective</b>                  | To devise, implement and evaluate a medication adherence support service by community pharmacists for elderly patients living at home and at risk of non-adherence.                                                                                                                                         | To assess patients adherence to new medication, identify how soon after being prescribed new medication non-adherence starts, explore medication related problems and assess information needs.                     |
| <b>Population characteristics</b> | 143 patients recruited from six pharmacies in Leeds.<br><br>Patients 65 years +, prescribed 4 or more medications and living alone.                                                                                                                                                                         | 258 patients across 23 community pharmacies in South East England.<br><br>Patients aged 75 years or older with one of the following chronic conditions, stroke, CHD, asthma, diabetes, RA.                          |
| <b>Intervention</b>               | Home visit by a community pharmacist to review medication and devise action plan and undertake structured questionnaire followed by follow up home visit by same pharmacist before next repeat prescription was due.<br><br>Interview by study co-ordinator at home at 8 weeks after 2 <sup>nd</sup> visit. | Telephone interview by researcher 10 days and at 4 weeks post recruitment.<br><br>Recruitment through presenting at pharmacy with a prescription for new medication for a chronic condition.                        |
| <b>Recruitment</b>                | Opportunisticly when presenting with a prescription at pharmacy.                                                                                                                                                                                                                                            | Opportunisticly when presenting with a prescription at pharmacy.                                                                                                                                                    |
| <b>Adherence definition</b>       | Reported rarely or never to 5 statements about non-adherence.                                                                                                                                                                                                                                               | Any missed doses of prescribed medicines within the previous 7 days.                                                                                                                                                |
| <b>Adherence measures</b>         | Self reported adherence developed from validated tool. Responses could be very often, often, sometimes, rarely or never.                                                                                                                                                                                    | Partial non-adherence - missing 1 or more doses of medication.<br><br>Complete non-adherence – stopping prescribed medication completely without consulting GP.<br><br>Intentional and unintentional non-adherence. |

Table 2: Surveys and service evaluations

|                                   | Raynor DK<br>et al 2000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Barber N<br>et al 2004                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Other measures                    | <p>Number of prescribed regular medicines</p> <p>Knowledge of purpose of medicines</p> <p>Number and nature of medicine related problems</p> <p>Direct costs to the NHS</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <p>Problems with medications</p> <p>Information needs</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Results of adherence measures     | <p>Significant improvement in non-adherence 62% to 86% (<math>p &lt; 0.001</math>)</p> <p>Cost effective – projected savings of £52 per patient per year (assuming that the intervention is made annually).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <p>Overall 38% (n=85) patients were non-adherent to at least 1 medicine.</p> <p>Non-adherence at 10 days= 30% patients still taking medication (n=67/226).</p> <p>Non-adherence at 4 weeks = 25% patients still taking medication (n=43/171).</p> <p>At 10 days 55% of non adherence and 56% at 4 weeks.</p>                                                                                                                                                                                                                                                                            |
| Confounding factors / limitations | <p>Potential for recruitment bias as pharmacist identified patients for recruitment from GP list and pharmacy PMR. Patients living alone identified from local knowledge. From this list a random sample of 30 were selected to minimise bias but not eliminate it.</p> <p>No definition of adherence reported in the study.</p> <p>Data on adherence self reported by means of answering rarely or never to questions about adherence at baseline and after intervention introducing potential bias.</p> <p>A higher proportion of female patients were recruited to the study (n=122) compared with male (n=39) making it difficult to draw overall conclusion across genders.</p> | <p>Range of limitations and bias noted by authors.</p> <p>Opportunistic sampling and recruitment of self reporters.</p> <p>Self reporting itself underestimation true non-adherence.</p> <p>Drop-out rate 7% (n=19/258) at 10 days and 23.6% (n=197/258) at 4 weeks.</p> <p>Study reported to identify causes of non-adherence as an outcome measure. A range of problems caused by medicines identified it did not report in detail the proportion of each problem in the adherent or non-adherent group making it difficult to draw conclusions with medicines and non-adherence.</p> |

Table 2: Surveys and service evaluations

|                 | Raynor DK<br>et al 2000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Barber N<br>et al 2004                                                                                                                                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                 | <p>Drop-out was relatively low at 12% ( n=18) but the proportion was higher in male patients 23% (n=9) compared with female at 7% (n=9).</p> <p>Study length and design limited (small sample over 1-2 month period) and noted as limitation by author.</p> <p>Clinical outcomes reported to be outside of the scope of the study due to wide range of conditions being treated.</p> <p>Generalisability questionable (author noted) as 6 participating pharmacies self selected from 154 pharmacists</p> |                                                                                                                                                                                                                                                        |
| <b>Comments</b> | <p>This study shows that community pharmacists can target patients at risk of medication non-adherence and using a structured approach identifies problems and implements solutions.</p>                                                                                                                                                                                                                                                                                                                  | <p>Significant proportion of patients taking new medication for chronic conditions become intentionally non-adherent.</p> <p>Many individuals need support and further information – high proportion of drop-out at 10 days increasing at 4 weeks.</p> |

Table 3: Literature reviews

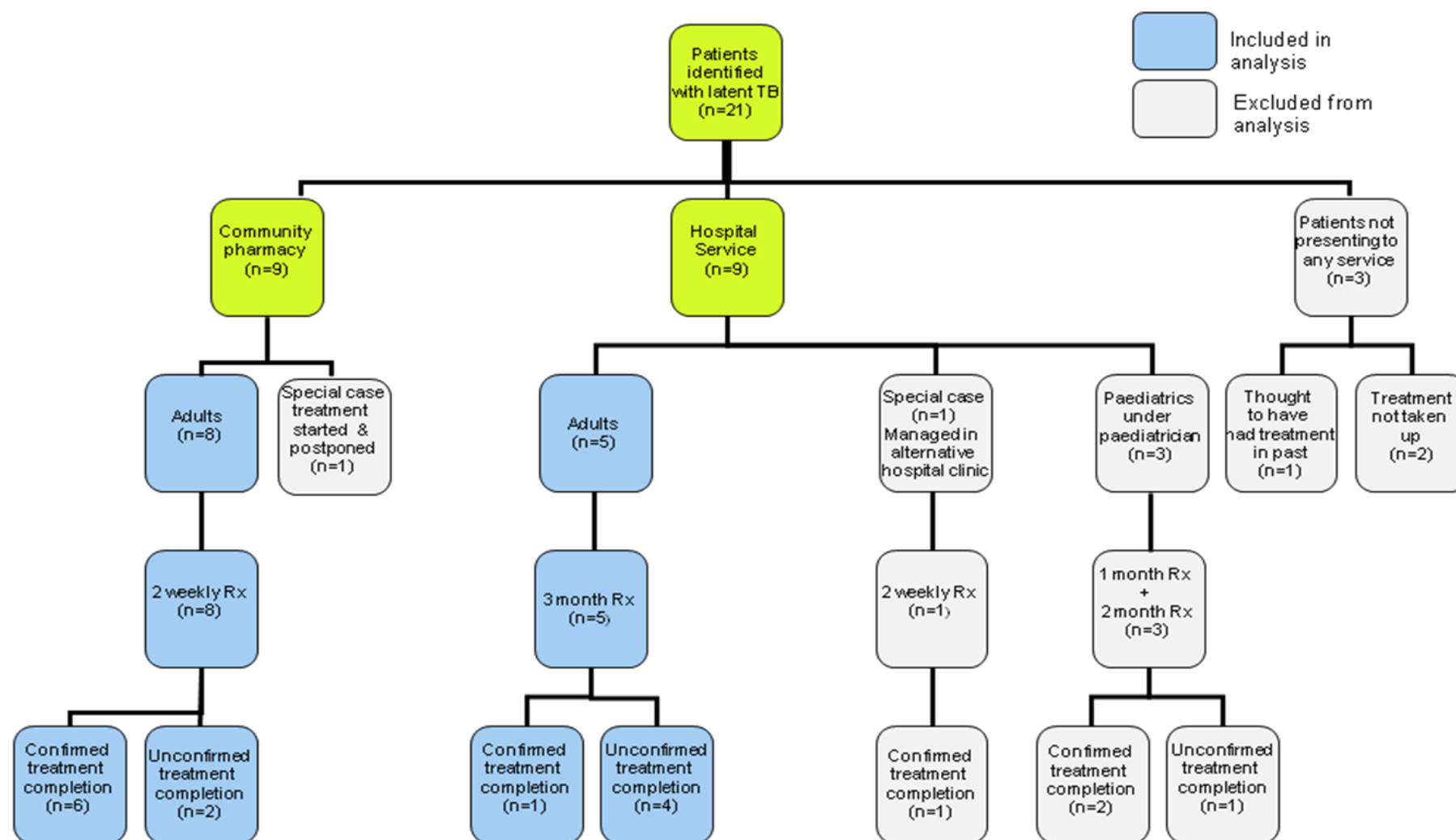
|                                       | Haynes RB et al<br>2008 (Cochrane) <sup>23</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                     | Clifford S et al<br>2010 <sup>24</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Study design</b>                   | Literature review                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Literature review                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Objective</b>                      | To update the 2005 Cochrane review of randomised control trials of interventions to help patients follow prescriptions for medications.                                                                                                                                                                                                                                                                                                                                              | To review and identify policy, education and research related to community pharmacy adherence services in England.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Search criteria</b>                | Overall review 1 September 1993 - 30 January 2007<br><br>Update 2005 – January 2007                                                                                                                                                                                                                                                                                                                                                                                                  | Publications between 2000 - 2010<br><br>Undertaken in England<br><br>Community pharmacy or community pharmacist<br><br>Compliance or adherence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>Database used</b>                  | The Cochrane Library, MEDLINE, CINAHL, EMBASE, International Pharmaceutical Abstracts, PsycINFO, Sociological Abstracts (CSA).                                                                                                                                                                                                                                                                                                                                                       | MEDLINE, EMBASE, International Pharmaceutical Abstracts, Pharmline. Reference list of relevant articles to find linked studies.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Findings relevant to adherence</b> | 78 RCT studies of which 21 are new studies since the earlier Cochrane review by Haynes 2005:<br><br>11/78 studies involved a pharmacist intervention <sup>31-41</sup><br><br>8/11 pharmacy intervention studies were for patients with chronic conditions, 1 for elderly patients (over 75 years) taking four or more medications and probable chronic condition/s and 2 for short term treatments for acute conditions.<br><br>2 studies were undertaken in the UK <sup>34,38</sup> | 8 studies (9 articles) found in the review falling into 4 broad categories of i) compliance aids ii) patient tailored interventions iii) education iv) discharge domiciliary service.<br><br>All studies identified were conducted in UK (England) and in a community pharmacy setting – as per search strategy.<br><br>3/9 studies reported on the involvement of community pharmacists with compliance aids, 1/9 study reported on the community pharmacist role in educating patients about effective use of a medication 4/9 studies assessed the effectiveness of a community pharmacist intervention on adherence <sup>15,17,19,22,34</sup> |

Table 3: Literature reviews

|                      | Haynes RB et al<br>2008 (Cochrane) <sup>23</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Clifford S et al<br>2010 <sup>24</sup>                                                                                                                                                                                                                                                                                                                                                 |
|----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                      | No studies were conducted in a community pharmacy setting. One study <sup>34</sup> used a community pharmacist in a domiciliary setting.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1/9 study assessed the effectiveness of a community pharmacist at discharge by mean of a domiciliary visit. <sup>34</sup><br><br>3/9 studies reported in 4 articles assessed the effect of a patient tailored intervention <sup>15,17,19,22</sup>                                                                                                                                      |
| Limitations/<br>bias | Review only looked at RCTs resulting in the small number of studies found in UK and in community pharmacy.<br><br>Most studies were quite small and only 1/8 pharmacist interventions were suitably powered to test effectiveness.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Review limited to studies in England only and does not identify studies undertaken elsewhere in UK.<br><br>Sample sizes for the majority of studies were small and with drop-out factored in all studies rendered underpowered.<br><br>Review one part of larger publication also reporting on policy and education provision influencing community pharmacy and medication adherence. |
| Results              | Review covered a range of interventions in various settings not specifically pharmacist interventions or community pharmacy settings resulting in 78 RCTs assessed.<br><br>Of the 78 studies 21 were new (published since the 2005 review).<br><br>Generally studies tended to be conducted for patients with chronic conditions with only 2 new studies assessing acute conditions.<br><br>There was insufficient common ground between studies due to variations in condition, setting, intervention, measures and reporting that a summary across studies could not be undertaken.<br><br>Results are presented whether there was a statistical difference between groups for adherence for each trial and no pooled data is available. | None of the compliance aids studies directly measured adherence – were descriptive studies on use of compliance aids.<br><br>2 RCTs <sup>15,17</sup> and 1 survey <sup>22</sup> on patient tailored interventions reported a significant improvement in adherence.<br><br>The 1 RCT on discharge domiciliary service showed no effect on adherence. <sup>34</sup>                      |

Table 3: Literature reviews

|          | Haynes RB et al<br>2008 (Cochrane) <sup>23</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Clifford S et al<br>2010 <sup>24</sup>                                                                                                                                                          |
|----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|          | <p>Of the 11 pharmacy RCTs only 3 reported a significant difference in adherence rates between intervention and control groups.<sup>33,37,38</sup></p> <p>Only one of these was a UK study and not conducted in community pharmacy setting<sup>34</sup> reporting a significant difference in adherence rates between intervention and control groups.</p> <p>Of the 3 studies reporting statistical significant differences in adherence rates between groups, two studies<sup>33,37</sup> reported a significant difference in clinical outcome measurements for patients with hypertension and hyperlipidaemia.</p> <p>One study<sup>33</sup> claimed that from the increase in adherence rates a significant difference in systolic blood pressure was observed in the intervention group and a statistical difference was also found according to a range of clinical outcomes.</p> |                                                                                                                                                                                                 |
| Comments | <p>For short term treatments several simple interventions increased adherence and patients outcomes but effects inconsistent between studies.</p> <p>For chronic conditions interventions were complex and not very effective. High priority should be given to research concerning interventions to assist patients to follow medication prescriptions for long term conditions.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <p>In England research to evaluate the effectiveness of community pharmacy support to patients with adherence is limited.</p> <p>There is a lack of studies and further research is needed.</p> |



## Summary of costs used for Cost Effectiveness Analysis

Table 1: Summary of costs of both services

| Resources                       | Costs in £                    |                                             |                 |
|---------------------------------|-------------------------------|---------------------------------------------|-----------------|
|                                 | Community Pharmacy Service    | Hospital Service                            | Total           |
| Costs of setting up the service | Manpower provided free by PHW | Nil as existing service                     | Nil             |
| Training costs                  | Nil                           | Nil                                         | Nil             |
| Service costs                   | £546.76                       | £490.05                                     | £1036.81        |
| Other costs (travel etc)        | Not identified                | Travel costs incurred but value unavailable | Not identified  |
| <b>Total cost</b>               | <b>£546.76</b>                | <b>£490.05</b>                              | <b>£1036.81</b> |

Table 2: Breakdown of service cost per patient for the community pharmacy service

| Service costs of community pharmacy service |                                 |                    |                             |                                           |
|---------------------------------------------|---------------------------------|--------------------|-----------------------------|-------------------------------------------|
| Patients                                    | No of weeks medication supplied | Monitoring fee (£) | Drug costs @ £5.84 per week | Dispensing fee @ £1.61 per item = 2 weeks |
| Patient 1                                   | 3                               | 10                 | 17.52                       | 3.22                                      |
| Patient 2                                   | 12                              | 10                 | 70.08                       | 9.66                                      |
| Patient 3                                   | 12                              | 10                 | 70.08                       | 9.66                                      |
| Patient 4                                   | 12                              | 10                 | 70.08                       | 9.66                                      |
| Patient 5                                   | 12                              | 10                 | 70.08                       | 9.66                                      |
| Patient 6                                   | 4                               | 10                 | 23.36                       | 3.22                                      |
| Patient 7                                   | 3                               | 10                 | 17.52                       | 3.22                                      |
| Patient 8                                   | 12                              | 10                 | 70.08                       | 9.66                                      |
| <b>Total</b>                                | <b>70</b>                       | <b>£80</b>         | <b>£408.80</b>              | <b>£57.96</b>                             |
| <b>TOTAL COST (£)</b>                       |                                 | <b>546.76</b>      |                             |                                           |

## Appendix 5 continued

**Table 3: Breakdown of service cost per patient for the hospital service**

| Service costs of hospital service |                                 |                                              |                                    |                                        |                           |                                    |
|-----------------------------------|---------------------------------|----------------------------------------------|------------------------------------|----------------------------------------|---------------------------|------------------------------------|
| Patients                          | No of weeks medication supplied | No of hours of TB nurse for visits /contacts | Cost of TB nurse time@ £19.77 / hr | Cost of consultant time @ £60 per hour | Drug costs @ £5.42 / week | Dispensing cost @ £5.00 per supply |
| Patient 1                         | 12                              | 2                                            | 39.54                              |                                        | 65.04                     | 5.00                               |
| Patient 2                         | 12                              | ½                                            | 9.88                               |                                        | 65.04                     | 5.00                               |
| Patient 3                         | 12                              | ½                                            | 9.88                               |                                        | 65.04                     | 5.00                               |
| Patient 4                         | 12                              | 1 ½<br>1 delivery                            | 29.65<br>19.77                     |                                        | 65.04                     | 10.00                              |
| Patient 5                         | 4                               | ½                                            | 9.88                               |                                        | 21.68                     | 5.00                               |
| <b>Total</b>                      | <b>52</b>                       | <b>6</b>                                     | <b>£118.66</b>                     | <b>£60</b>                             | <b>£281.84</b>            | <b>£30.00</b>                      |
| <b>TOTAL COST (£)</b>             |                                 | <b>£490.05</b>                               |                                    |                                        |                           |                                    |

