Senga Steel

A study of Tuberculosis in an urban community with particular reference to sunlight exposure and Vitamin D status

Submitted to University College London for the degree of PhD

September 2012

Declaration

I declare that all work included in this thesis is my own, and was conceived and carried out exclusively by myself, other than the following chapter, which was the result of conjoint work with the Brent Refugee Forum:

Knowledge, perception, barriers and the social meaning of Tuberculosis among asylum seekers, the homeless and refugee communities in Brent

In this project, I acted as the academic supervisor throughout, from its conception to completion. I advised on every stage of the project development, including the research protocol, methods selection, analysis techniques and questionnaire and focus group schedule design and the final write-up. I was advisor to the volunteers, who were recruited to undertake the focus group sessions, and provided the teaching for them to undertake this role. The volunteers were recruited by Dr Amna Mahmoud, from the Brent Refugee Forum who sponsored the study. I undertook some of the interviews of professional staff, analysed the transcripts and contributed to the final write up of the project for the Sponsor organisation. Dr Mahmoud was responsible for securing the funding for this research, which was provided by Brent PCT and co-ordinating the study. Other investigators included Ms Kultrum Osman Rivers, from the CK consultancy group, who was recruited to provide a third investigator to analyse the transcripts to ensure a rigorous approach to analysis and findings.

The IGRA tests were undertaken by Jennifer Harvey, Clinical Scientist at the Department of Clinical Immunology, Royal Free Hospital, London. The 25(OH)D assays were undertaken in the clinical biochemistry department of the Northwick Park Hospital, London.

I declare that all other work was completed solely by me.

I, Senga Steel confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed .....
Senga Steel

Abstract

This thesis presents a mixed method study of urban Tuberculosis, with reference to both social and physical factors. The initial study reports the social context of Tuberculosis in Brent, London. 104 subjects participated in focus group discussions from community organisations. Knowledge, perception and barriers to Tuberculosis treatment were explored. Participants included refugee, homeless and immigrant groups. A thematic analysis revealed stigma, memory of home life, knowledge of disease and Tuberculosis as 'divine punishment' as significant social factors. The professional groups reported language, patient expectations and the fragmentation of services as barriers to successful treatment.

A second study explored the relationship between sunlight exposure and Vitamin D status in Tuberculosis cases and contacts. UVR exposure was measured using Polysulphone film over 8 weeks in an urban setting. Median values for 25(OH)D in index cases were 23.5 nmol/l and 33.0 nmol/l in contacts cases, at the end of the study period. Sun exposure was not significantly related to 25(OH)D in index cases (r=0.016, sig=0.961, p=0.05) and showed only a weak positive correlation in contacts (r=0.233, sig=0.44, p=0.05). No seasonal variation was evident in either group. The requirement to wear a film badge prevented some subjects taking part as this was perceived to be stigmatising. This was an unexpected finding. Only 12 index cases and 13 contacts completed the study.
Finally, ambient UVR levels were measured in London and these data compared well with measurements from a rural site, suggesting that the potential for sun exposure is similar in both rural and urban settings.

The stigma of Tuberculosis hinders treatment success as well as engagement with clinical research. Language difficulties and fragmentation of services make access and treatment completion challenging and complex. The built environment and lifestyle factors may influence the opportunity to obtain sufficient sunlight for Vitamin D sufficiency in those with Tuberculosis. Whether lack of sunlight causes Vitamin D deficiency requires further study.

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Acknowledgements

I would like to thank the following people without whom, it would not have been possible to complete this thesis.

Dr Amna Mahmoud, formally of the Brent Refugee Forum, and all of the volunteers from the community groups, who led the focus groups in the Brent study. I would also like to thank the community members who took part so enthusiastically in the focus groups discussions about Tuberculosis. Thank you to the Brent Refugee Forum who sponsored the study and the Burdett Trust for Nursing who generously provided the grant funding for the sunlight and Vitamin D study. Thank you also, to all the patients who took part in the sunlight study.

The following people have been invaluable in their support in this research:

Professor James Malone-Lee, my supervisor, for the years of support, kindness and teaching. Dr Norman Johnson, consultant chest physician. Molly Mamdani and Mary McDaid, clinical nurse specialists at Whittington Health. Dr Adrian Martineau, Queen Mary's School of Medicine and Dentistry, for his advice and support. Thanks to Deborah Wheeler, formally Director of Nursing at Whittington NHS Trust, who supported me in conducting this work whilst I was assistant director of Nursing in her directorate. Thank you to Bronagh Scott, current Director of Nursing for her continued support. Thank you to Brian Diffey, Emeritus Professor, Newcastle University, who provided invaluable advice and guidance on UV measurement and Dr Alastair McKinley, of the National Radiological Protection Board, for early advice on methodological issues. Thanks also to Richard Peacock, Clinical Librarian for his years of support and Sara Callen.

Thanks to Liz Denver, senior nurse at UCL, for her support in all kinds of ways too numerous to mention. Thank you to Sanela Andrijac, my PA, who was always ready to listen. Thank you to Dr Amir Ahmed, of the Urological laboratory at UCL Riding House Street, for the use of his laboratory and equipment.

Last, but by no means least, thank you to my father and my brother for their continued support over the years and for their encouragement and understanding. To Susan Dart, for her unending kindness, advice and patience. Lastly, I would like to thank

my partner, Paul Varney, whose love, friendship, enthusiasm and tolerance were central to my success in completing this research. He remains an inspiration to me, in his example of these qualities, and their continued value in our lives together.

1 Chapter 1: The captain of all these men of death: the problem of Tuberculosis in London

1.1 Introduction

Tuberculosis has plagued humanity throughout history and prehistory yet contrary to popular belief, it is not a disease that is confined to the past. Tuberculosis is caused by the Tubercle Bacillus, a bacterium from the Mycobacterium family of microorganisms (*Mycobacterium tuberculosis*). It can affect any part of the body including the lymph glands, the spine (Pott's disease), the lungs and other organs. Common sites of the disease can be viewed in Table 1(1). When a person has a dominant infection of the lungs, he/she is often described as having open Tuberculosis and is most infectious in this state. The disease is spread by the 'atomisation' (aersolisation) of respiratory moisture when an infected person coughs and another inhales the bacillus. Atomisation is the principal process by which aerosols are formed, following high pressure expulsion of air through the moist and narrow structures of the respiratory tract(2). Coughing and sneezing expel the bacteria, containing them within a liquid shell, that when evaporate form bacterial droplet nuclei that are suspended within the atmosphere of indoor environments(3). These miniature suspended life forms have varying life spans and falling rates, so are easily inhaled by room inhabitants(3). Tuberculosis continues to be one of the principal causes of death from an infectious disease worldwide, regardless of the fact that the majority of strains are completely treatable and curable(4). It therefore remains a worthwhile area of scientific investigation in terms of its persistence and its remedy.

This thesis will explore the problem of Tuberculosis with particular reference to the urban environment. It will consider the social, cultural and physical consequences that living styles and urban life may have on the prevalence and incidence of disease and the challenges each of these areas of influence present to the successful treatment of Tuberculosis. It will explore risk factors that increase the likelihood of transmission and infection as well as the challenges for future clinical research in this field. It will argue that the impact of urban life is an important contributor to disease risk in contemporary life, as much as it was in the past. Each chapter will address a specific research question relevant to urban life and Tuberculosis and have been

drawn from the body of literature that currently supports knowledge in this field. When the outcomes of these questions are considered together, they provide an insight into problems of Tuberculosis in the urban environment and its contemporary resurgence.

Table 1: Tuberculosis case reports by site of disease, UK, 2009

Site of disease*	Number of cases	Percentage**
Pulmonary	4,851	54.1
Extra-thoracic lymph nodes	1,831	20.4
Intra-thoracic lymph nodes	810	9.0
Other extra-pulmonary	694	7.7
Pleural	620	6.9
Gastrointestinal	367	4.1
Bone – spine	364	4.1
Cryptic/miliary	258	2.9
Bone – other	180	2.0
CNS – meningitis	179	2.0
Genitourinary	118	1.3
CNS – other	91	1.0
Laryngeal	17	0.2
Unknown extra-pulmonary	13	0.1

* With or without disease at another site

** Percentage of cases with known sites of disease (8968)

CNS - Central Nervous System

Total percentage exceeds 100% due to infections at more than one site

Table provided by the TB section of the Health Protection Agency. Reproduced with permission of the HPA centre for infection.

1.2 Global view

It is estimated that one third of the world's population is infected with *Mycobacterium tuberculosis (MTB)*(5) with a disease ratio of about 10% (6). It has been reported that every year 8-10 million new cases arise and 2-3 million of these will eventually die (6).The large majority of people who have become infected with MTB will remain well with the bacteria staying latent in the body. This state is referred to as latent Tuberculosis infection (LTBI). Since it is difficult to predict who and why some

people develop overt disease and others do not, scientists and health workers have sought to unravel what these circumstances might be, in order to alleviate the great human suffering brought by '*this captain of all these men of death'* in the famous words of John Bunyon.

1.3 The Town and the City

The environment in which we live presents significant risk factors that affect the changing epidemiology of Tuberculosis. Urban environments, even in the developed world, bring together factors that have been shown to significantly influence transmission possibilities for infectious diseases and other health problems(7). By their nature towns and cities are frequently overcrowded and are often home to some of the poorest communities. Large numbers of people migrate to urban areas in search of employment, opportunities and better lives. Increased population density, unemployment, poor housing and specific population demographics, including those from high prevalent countries, all contribute to the increased risk of Tuberculosis (8-10). These factors also, collectively, make up recognised indices of poverty and deprivation.

Three broad mechanisms affect the possibility of acquiring Tuberculosis. The first relates to the robustness of the host immune response and the ability to fend off infection. The single most important host factor contributing to the global increase in Tuberculosis is believed to be HIV infection, due to the effect the virus has on human immunity(6),(11). Other factors that affect host immune resilience include neutropenia, malnutrition, renal failure, liver failure and measles in children (6). The second relates to the virulence of the organism in question and its ability to adapt and resist host defences. The third relates to the environment in which the host resides, the social and environmental context that presents the opportunity of exposure to the bacteria itself. All three contribute to the epidemiology of Tuberculosis and, within each sphere; there are complex mechanisms at play that determine risk of infection and progression to overt disease. Additionally, individual behaviour such as smoking(12), illicit drug use(13) and heavy alcohol consumption (14), have also been identified as important risk factors. Perhaps it is no coincidence that these social behaviours also feature strongly in areas that are socially deprived.

1.4 Housing

Poor housing has long been recognised as an important determinant of general health and has been shown to be a significant independent risk factor in the incidence and prevalence of Tuberculosis in towns(15),(16). This relationship is attributed to the level of crowding that increases the exposure possibilities to infection. Moreover, a strong positive association has been shown between Tuberculosis mortality and household overcrowding(11). Studies have suggested that for each 1% increase in the numbers living in overcrowded conditions this will average a 12% increase in notification rates(17). Early studies in Edinburgh and Glasgow showed that the number of cases of Tuberculosis increased in proportion to the decrease in accommodation size (16). Williamson found in densely populated cities in Scotland in the early 20th century that death rates from *'phthisis'* rose in almost direct proportion to the 'limitation' of the housing. He recorded 87 deaths in houses of four rooms or more, 106 in three, 179 in two and 222 per 100,000 in houses of one room. The same pattern was noted in other Scottish cities in which he examined these relationships. It is no coincidence that at the same time the childhood disease Rickets was also rife in Scottish and English cities, as the densely built towns often meant that children did not receive sufficient sunlight to make sufficient Vitamin D to calcify their bones. This relationship is interesting too, if we consider the germicidal properties of ultraviolet radiation (UVR) as exposure to UV in the 'B' range of the electromagnetic spectrum, is known to alter the deoxyribonucleic acid (DNA) of MTB and other living cells, preventing their reproduction and hastening their death(18). This relationship is unlikely however, to be significant in terms of the germicidal potential of UVR in houses, as window glass is known to filter out shorter wave UVR (UVB)(19). Ventilation in the home is likely to be of greater significance in diluting the concentration of droplet nuclei present in room air and therefore lessening the exposure potential to the host(20).

However, sunlight also contributes and instigates important physiological responses of the host and this too may be mediated by lifestyle, environment and the opportunity for exposure to light. City life potentially contributes to Tuberculosis risk through both physical and social factors and these interrelate to contribute to overall disease risk(8). This thesis will focus on sunlight exposure and its contribution to Vitamin D status as the physical host related risk factor of interest and also the social perceptions

of an at risk groups within a large city, and how these too might also influence successful diagnosis and treatment of the condition.

The next chapter will provide some historical background of the Tuberculosis problem in London, followed by a social exploration of the Tuberculosis problem in Brent, London. This study shall form the social contextual focus of this thesis followed by a study that examines the influence of sunlight exposure to a group of index cases and contacts in order to examine the significance of sunlight exposure on host Vitamin D status. The significance of Vitamin D status to the Tuberculosis story shall also be explored.

2 Chapter 2: Historic London

As this thesis will focus on the problem of Tuberculosis in London and the relative contribution of urban life it is, therefore, useful to briefly reflect upon an historical perspective of health and disease in London up to the present day.

In 1700s London the poorer areas of the city were defined by crime, depravity and poor health and this situation was not helped by the social habits of the poorer classes. Excessive gin drinking, for instance, was a popular pastime as it was cheap and available and offered some escape from the poor living conditions of the squalid and unhealthy slums. This did little, however, for the general health of the population. Additionally, houses were so tightly packed together that the term 'Rookeries' was adopted to illustrate the simile of a collection of rook's nests packed together(21).

2.1 Records of Mortality

It is not surprising, given these social and behavioural circumstances, that people died early in 1700s London. An examination of the London Bills of Mortality at the time reveals a disturbing array of morbid conditions. These 'bills of death' were collected by the Parish Clerks Company of London, who employed 'searchers of the dead' reportedly 'Sober and ancient women'(22), who went from door to door making enquiries of the deceased. Records began as early as the beginning of the 16th century with the cause of death being recorded from 1629, although some sources report a later date for vigilant record keeping. Table 2 details a typical year with Tuberculosis being a major cause of death, referred to by its various euphemisms, the prevalent term of the day being *'consumption'*. It is also thought that the category *'Evil'* refers to the *King's evil,* so called as it was thought that by touching the robes of Kings one would be cured of *'Scofula',* tubercular disease of the lymphatic system(23). It is important to note that the diagnosis of Tuberculosis and other forms of illness was not a sophisticated science at this time, and it is reported that for a small sum the searchers of the dead could be bribed to record a less shameful cause of death, if the person had died from syphilis for example(22). Even in 18th century London social attitude was a powerful force in shaping attitudes to illness. Tuberculosis was thought to afflict the weak in character, and would therefore not have been an attractive cause of death for families with social aspirations. Tuberculosis did not reach its 'romantic'

peak until the middle of the 19th Century, when it became known as a disease of the poetic and artistic, having claimed the lives of many well known literary figures(24). It was considered attractive and aesthetically pleasing to display the outward pallor and physical frailty of the Tuberculosis sufferer as these symptoms became symbolic of the artistic character(24). It was therefore possible that prior to this metaphoric conceptualisation of the disease, that people avoided the diagnosis in order to preserve their social reputation.

None the less, there are a high percentage of deaths related to tubercular disease recorded. The table shown here in Table 2 was adapted by Dr Craig Thornber from data originally published in the *Gentleman's Magazine* which was published from 1730 until 1914(25). The table is reproduced here with permission from Dr Thornber.

By 1750, approximately 15% of the UK population lived in towns and, by 1800, 80% of the population was urban(26). London saw an increase in its population at this time and between 1801 and 1841, the population grew from 800,000 to 1, 8000,000. By Queen Victoria's death this had increased to approximately 7 million(26). This pattern of expansion in population growth was not isolated to London but reflected a trend in human geography across urban Europe. Life expectancy in the city at this time was on average only 39 years compared with the rural areas, where people generally lived much longer.

In the 1800s the situation had not improved. UK life expectancy in early 1800 in the town and city areas was 35 years and this was reduced to 29 years, a decline that has been associated with the increase in population and density(27). The cities were witnessing new epidemics, following the demise of the Black Death, and these included Tuberculosis, Cholera and Typhoid, the latter being carried and transmitted by filthy water supplies(27). There was little investment in town planning and infrastructure such as improvements to sewage systems, street hygiene and decent housing, and indeed, these improvements did not occur until the public reforms of 1875, when the Public Health Act was introduced(27).

Descriptions of life in London at this time can be found in art and literature as these media offered the only channels of formal communication. One has to bear in mind that a level of poetic licence may have been employed in these often florid

descriptions but, none the less, they offer atmospheric insights into the level of poverty and filth prevalent in 1800s London. In this passage Charles Dickens observes the squalid conditions that were to be found in Victorian London in slums:

> *"Wretched houses with broken windows patched with rags and paper; every room let out to a different family, and in many instances to two or even three – fruit and 'sweetstuff' manufacturers in the cellars, barbers and red-herring vendors in the front parlours, cobblers in the back; a bird-fancier in the first floor, three families on the second, starvation in the attics, Irishmen in the passage, a 'musician' in the front kitchen, a charwoman and five hungry children in the back one – filth everywhere – a gutter before the houses, and a drain behind – clothes drying, and slops emptying from the windows; ... men and women, in every variety of scanty and dirty apparel, lounging, scolding, drinking, smoking, squabbling, fighting, and swearing.*
>
> Charles Dickens, *Sketches by Boz*, 1839 on St Giles Rookery (28)

Table 2: London Bills of Mortality: A Typical year 1730s London

Abortive and stillborn	546
Aged and bedridden	1242
Ague(malaria and other diseases with chills and fevers	676
Apoplexy-stroke	104
Beedling-bloody flux and flux	1
Cancer, canker and trush	124
Chicken pox	1
childbed	240
Chrisoms and infants	78
Colick	72
Consumption	**2819**
Convulsion	4631
Cough	7
Cut of the stone-(kidney stones, bladder stones)	43
Diabetes	1
Distracted and Lunatic	35
Dropsy and Tyranny	659
Evil	**83**
Executed	29
Falling sickness	1
Flox,smallpox and measles	1031
French pox	69
Gangrene, fistula and mortification	36
Gout and cramp	15
Grief	5
Griping in the guts	1004
Headache	1
Head-mould shot	6

Jaundice	73
Impostume (a festering boil or abscess)	59
	5
Lethargy	11
Livergrown	1
Looseness	69
Overlaid-baby sleeping in bed with parent accidently smothered	30
Palsy	31
Pleurisy	30
Quinsie (tonsilitits)	10
Rheumatism	16
Rickets	393
Rising of the lights	101
Rupture	18
St Anthonys fire	9
Scarlett fever	1
Scurvy	5
shingles	1
Sores and ulcers	62
spleen	3
Spotted fever and purples	189
Stoppage in the stomach	320
strangury	9
surfeit	70
Swelling in the neck	1
Teeth	1159
Twisting of the gut	2
Vapours and waters in the head	7
Vomiting	15
worms	53
bruised	1
Burnt and scolded	8
drowned	48
Found dead in the street	9
Hanged and made away themselves	28
Hanged by misfortune	1
Killed by accident	38
Murdered	11
Smothered and suffocated	3
Stabbed	1

Adapted by Dr Craig Thornber and reproduced with permission

2.2 Contemporary London

Today, London has the highest rates of Tuberculosis disease incidence in the UK accounting for just fewer than 40% of the total UK incidence(29). It is a densely populated urban environment, with a population of 7.5 million people of ethnically diverse origins, and a significant proportion of newcomers that have arrived from countries of high prevalence.

Since the 1980s there has been a gradual rise of Tuberculosis cases in the UK and, in 2009, there was a 4.2% rise giving an overall rate of 15 cases per 100,000(1). London however, accounts for 38% of all cases in the UK, with a rate of 44.4 per 100,000. Figure 1 shows the disease rates by region for England in 2009 with London displaying the highest rates(29). Figure 2 and Table 3 show UK rates with a further breakdown of the London picture, showing the boroughs of Newham and Brent as having the highest rates. In Newham and Brent the rates are double that of London as a whole, with rates as high as 116 per 100,000 of the population in Brent and 140 per 100,000 in Newham. Table 1 shows the most common sites of disease with pulmonary Tuberculosis being the highest in UK notifications.

Figure 1: Tuberculosis case reports and rates by region in England 2009

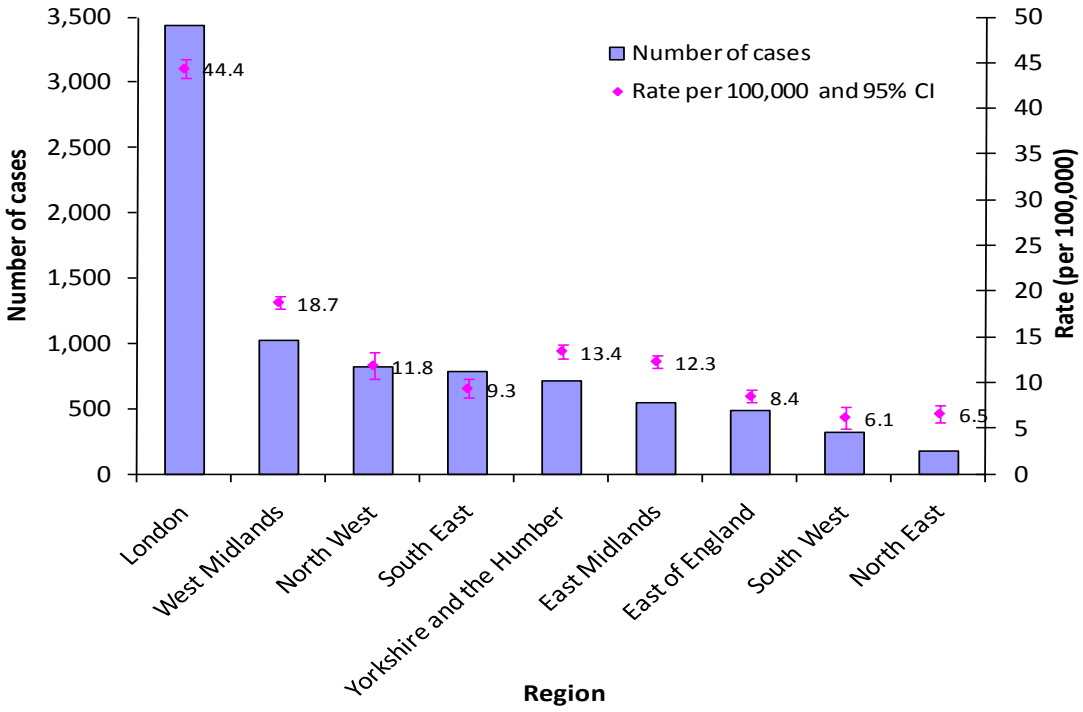
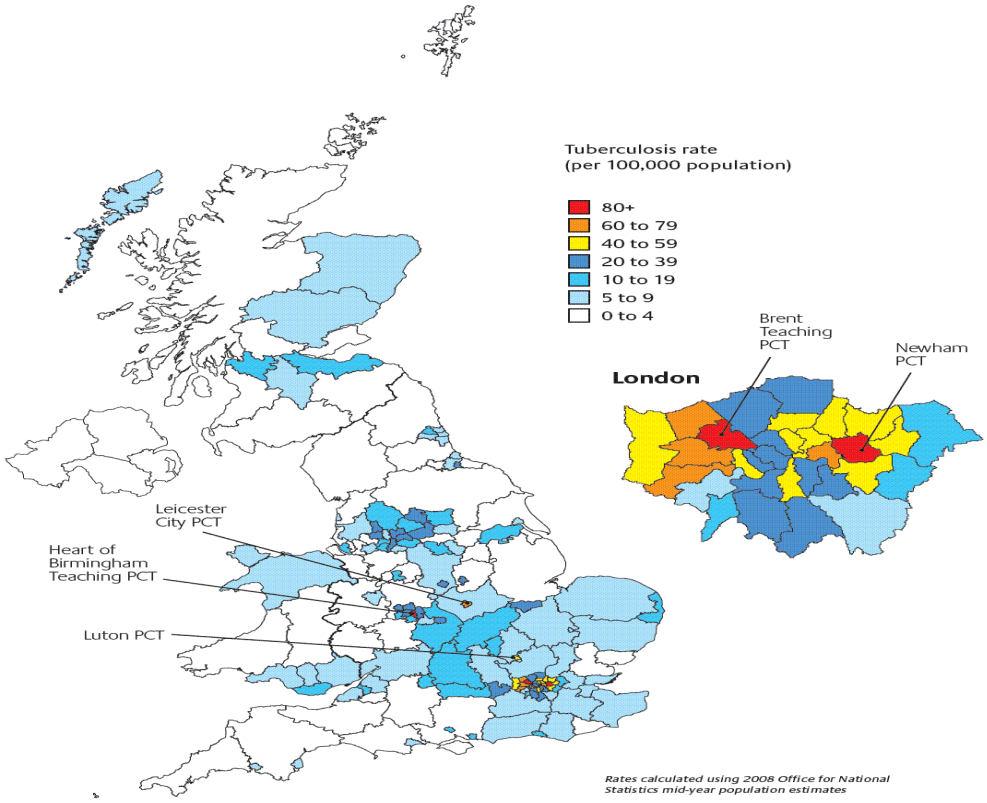


Table provided by the TB section of the Health Protection Agency. Reproduced with permission by the HPA centre for infection.

Figure 2: Three year average Tuberculosis case rates by primary care organisations UK, 2007-2009



* England – Primary Care Trusts (PCTs)
Northern Ireland – Health and Social Services Boards
Scotland – NHS Boards
Wales – Local Health Boards

Sources: Enhanced Tuberculosis Surveillance (ETS)
Enhanced Surveillance of Mycobacterial Infections (ESMI)
Office for National Statistics (ONS) mid-year population estimates

Figure provided by the TB section of the Health Protection Agency. Reproduced with permission by the HPA centre for infection.

Table 3: Rate per 100,000 population of new TB notifications in London residents by PCT of residence and year of notification - reported to the London TB Register

PCT	2005	2006	2007	2008	2009*	Yr ending 30/06/2010
North Central						
Barnet	35.9	37.4	31.5	34.4	32.0	35.9
Camden	45.3	42.6	38.4	36.1	42.4	36.5
Enfield	36.7	35.1	25.6	34.8	40.7	43.1
Haringey Teaching	58.9	67.8	41.4	45.5	57.9	57.0
Islington	47.2	52.3	49.5	48.7	47.7	46.1
North Central Total	**43.6**	**45.5**	**35.9**	**38.9**	**42.8**	**42.9**
North East						
Barking and Dagenham	36.3	29.6	37.1	40.9	43.2	43.8
City and Hackney Teaching	61.5	63.4	65.7	56.3	53.6	57.2
Havering	13.3	10.1	7.0	8.7	13.0	11.3
Newham	102.9	105.1	111.0	115.0	124.2	140.7
Redbridge	48.2	57.2	53.1	63.3	57.1	58.6
Tower Hamlets	61.6	62.5	71.1	60.3	65.3	76.2
Waltham Forest	51.7	54.6	41.4	57.8	42.1	57.8
North East Total	**54.9**	**56.2**	**56.5**	**58.9**	**58.3**	**65.3**
North West						
Brent Teaching	105.8	88.4	101.5	113.5	110.5	116.8
Ealing	78.2	76.7	77.3	62.5	71.8	79.3
Hammersmith and Fulham	52.6	46.7	39.4	39.5	43.0	45.3
Harrow	62.1	57.8	56.8	59.2	63.4	67.1
Hillingdon	57.7	50.4	50.7	60.0	48.6	57.7
Hounslow	77.1	63.1	61.7	60.2	77.7	90.3
Kensington and Chelsea	27.9	29.8	17.9	29.4	27.7	26.6
Westminster	42.0	36.7	36.7	29.2	34.7	36.4
North West Total	**65.7**	**58.7**	**58.5**	**59.4**	**62.4**	**68.0**
South East						
Bexley	10.4	8.6	11.7	9.4	7.6	8.5
Bromley	9.7	13.7	11.6	6.3	10.6	11.2
Greenwich Teaching	39.7	44.0	47.1	61.9	55.6	58.8
Lambeth	53.6	49.3	38.1	46.3	42.3	47.4
Lewisham	39.1	33.2	38.7	32.1	29.1	33.3
Southwark	51.9	46.4	37.9	42.1	34.2	42.1
South East Total	**34.1**	**32.6**	**30.5**	**32.4**	**29.4**	**33.1**
South West						
Croydon	33.7	30.3	34.5	32.8	36.3	37.7
Kingston	18.8	16.0	18.4	18.1	19.4	24.4
Richmond and Twickenham	10.7	11.1	7.8	7.2	11.7	13.3
Sutton and Merton	22.7	24.3	23.4	20.8	23.9	24.7
Wandsworth	45.2	29.4	40.8	38.7	29.6	32.7
South West Total	**28.1**	**24.1**	**27.1**	**25.5**	**26.1**	**28.1**
London Totals	**46.7**	**44.5**	**43.0**	**44.3**	**45.1**	**49.0**

Table provided by the TB section of the Health Protection Agency. Reproduced with permission of the HPA centre for infection. Tables sourced from(29).

Ovals in table highlight annual rates per 100,000 population for Brent from 2005-2010.

3 Chapter 3: Knowledge, perception, barriers and the social meaning of Tuberculosis among asylum seekers, the homeless and refugee communities in Brent

Epidemiological data shows that Brent was experiencing disproportionately high rates of Tuberculosis; almost double that of some other parts of London. Given this 'hot bed' of active disease, it would seem an ideal place to start investigating the problem. I wondered what was special about Brent, compared with other parts of London that dictated such high rates of Tuberculosis notification. What problems existed in terms of treatment and identification of disease? How were the social conditions contributing to the public health picture in Brent with regards Tuberculosis incidence? And how could the problem of Tuberculosis be addressed to reduce these very high rates? Data already existed about the incidence and prevalence of Tuberculosis in this borough but what was not known was how the people themselves viewed the problem? Understanding of this nature is vital if solutions are to be found that are based upon the social and cultural realities of the communities affected by Tuberculosis and their relationships with the providers of health care.

3.1 The Brent population

A large proportion of the Brent population is made up from Black and Minority Ethnic (BME) groups and is the second highest ethnically diverse borough in the UK(30). Figure 3 shows the configuration of these groups reported in 2010(31). Approximately 130 languages are spoken in schools in Brent and it has the highest proportion of people born outside the EU in England and Wales(30;31).This is particularly significant in the context of the high numbers of Tuberculosis notifications as Brent also has a high degree of immigrant and refugee communities that have travelled from countries where the incidence and prevalence of Tuberculosis is high among the indigenous populations(30).The majority of cases within the borough and indeed within the UK are from those whose place of birth is not the UK or there are other significant co-existing risk factors, such as co-infection with HIV and homelessness(30;32).

3.2 Definitions

Asylum seekers, refugees and homeless persons have specific health requirements and are at greater risk of poor health in general(33). A person who seeks asylum is 'someone who has sought refuge in another country owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a political or social group, or political opinion, or is unable to return to a country due to this fear(34). Asylum seekers who receive a positive decision on their claim acquire refugee status(34).

Statistics taken from the Brent refugee strategy report refugee numbers between 16,300 and 18,800 refugees in Brent based on 2001 Mori figures(34). This equates to between 6.5 and 7.5% of the population. However, it was estimated at this time that the actual number was as many as 20,000. These figures represent one of the largest refugee communities in the country. In Brent and other areas where refugee and asylum seeker status is high there is often a high degree of associated homelessness, as many people who enter the country as a result of political asylum have nowhere to go or only have temporary accommodation(35). Definitions of homeless people include a complex set of definitions that include those with 'no fixed abode', 'rooflessness', rough- sleepers, as well as those living in hotels, hostels and temporary accommodation(36).

3.3 Health problems among asylum seekers, refugees and homeless groups

There is little research in the UK that has been undertaken specifically addressing the health needs of refugees(37). This is thought to be the case because it does not represent an immediate health concern for the general population but this does not diminish the very real and acute health needs of these groups(33). Many of the health problems of refugees are not necessarily specific to refugee status, but overlap with health problems related to deprivation and poverty frequently experienced by excluded or black and minority groups (BME) (37). Some health problems are anecdotally associated with traumatic history, torture, loss of status and culture change(37). Additionally, fear of persecution and actual physical abuse all contribute to the overall health status of these individuals who by their very status are people in crisis(33). In terms of infectious disease, such as Tuberculosis, the epidemiology of any area is influenced by the origins of its people. Brent has both a high degree of

refugees and residents who were not born in the UK and who have originated from areas of the globe, where Tuberculosis is both endemic and epidemic.

Among asylum seeking populations entering the UK, the prevalence of Tuberculosis during a screening programme at a busy London airport was as high as 241 per 100,000(35). The highest rates were among those people originating from sub-Saharan Africa and the Indian subcontinent. This study did not account for those people who may have already been infected at an earlier stage in their country of origin and may go on to develop active disease in the future. A high degree of drug resistant Tuberculosis was also present in refugee communities entering the UK in this study(35). Figure 3 shows how these two groups in particular are reflected in the Brent demographic profile with 33% of the population being of 'Indian' origin and 14% as black African.

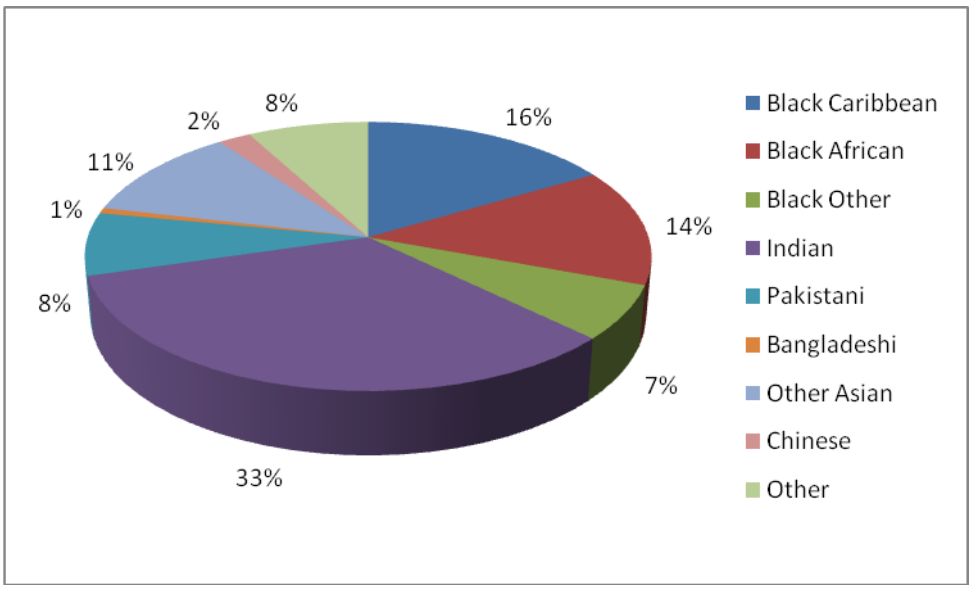
Among homeless populations, misuse of alcohol, illicit drug use and heavy tobacco consumption are higher than among the general population and these behaviours increase the risk of Tuberculosis(38). Poor physical health among this group coupled with poor hygiene and poor living conditions results in a high risk of infectious disease in general(36;38). At the time of undertaking this research, Brent had the second highest levels of homelessness in London.

3.4 Brent and deprivation

Brent was, and still is, one of the most deprived authorities in England, ranking 11th in 366 local authorities in England(39) and ranks 7th most deprived in terms of the severity of deprivation at the time of the last census in 2001(39;40). In order to understand what this means in social terms it is important to briefly outline how deprivation is classified and measured in a census. The indices of deprivation include measures of household income, ranking of employment, health status, educational achievement, housing conditions, crime rates and living environments (2001 census). It is therefore a useful reflection of poverty. Measures of these indices in Brent show a high degree of overcrowding and population density (61 persons per square hectare compared with 46 per square hectare in inner London)(40). It is also one of the most heterogeneous boroughs in Europe, in terms of its ethnic and cultural diversity (Figure 3). A high degree of deprivation and numerous ethnic minorities are known risk

factors for increased levels of Tuberculosis incidence. Incidence figures for Brent have continued to rise and recent figures show that they are still among the highest in London with a notification rate of 299 in 2009(29).

Figure 3: Ethnic distribution of Brent population



Sourced from Brent Council Borough profile 2010(31) Reproduced with permission.

At the time when this research was undertaken, there was a great deal of focus on 'at risk groups' and this was partly driven by the publication and directive of London quality metrics for the control of Tuberculosis(41). One of the targets stated that patients displaying signs and symptoms of Tuberculosis should be referred and seen by a chest physician within two weeks(41). Completion of treatment was also high on the agenda, given the relationship with poor treatment adherence and the emergence of multi drug resistant strains of the disease(42). These quality metrics led to interest within the clinical community to explore and understand the delays to diagnosis that may occur from within the system, as a result of service design and from within the communities at risk, who may not seek help for a variety of reasons that could potentially delay diagnosis. This focus on understanding the experience of Tuberculosis in order to improve the provision and possibility of successful treatment focused my approach to this research.

3.5 Literature review

A literature review was undertaken to examine how elements of 'social' and community life might be affecting the perceptions and responses to disease among a London community. But what was 'social' life and what aspects of it might be important? I had to first decide how these concepts might be reflected and operationalised in the literature in order to allow the search to identify significant and informative papers. To begin, I selected terms identified as important in both the public health surveillance data for London(32) and the London stop Tuberculosis action plan(41) and other broad terms that might be used to describe social and community life . These included first identifying elements of individual experience such as 'perceptions', 'social', 'meaning', 'culture' and 'knowledge' and where these elements of community and social life might form 'barriers' and inhibiters to successful treatment and case identification. Where a concept was particularly complex to unravel or difficult to know how its various elements might be expressed or how they might contribute to disease, these terms were exploded, for example 'culture'. Secondly, I considered key terms that would help identify the target groups and how these factors might also contribute to responses to disease. I therefore included terms in the search strategy that could describe the groups of interest such as 'refugees', homeless persons' and 'asylum seekers'. Finally the search terms needed to include the term Tuberculosis and TB and the location of the study (London, UK), in order to identify local work upon which further study could inform.

3.6 Search strategy and study selection

Following selection of the search terms a search strategy was constructed. The full search strategy can be viewed in appendix 1. Both CINAHL and MEDLINE databases were searched from their start date up until the year 2006. No limitations by language were employed in the search. A search of the internet was also conducted. The search strategy was designed to provide evidence around previous work that had addressed similar issues, in London, UK. Whilst one study conducted in the USA was included, most studies that explored these questions in other parts of the world were excluded from this review. The USA study was included because it was one of the few studies that employed purely qualitative interviews of an immigrant group in an inner city environment likely to be reasonably comparable with UK inner city environments and

incorporated all of the search terms. Whilst there were many studies that explored these questions globally, the experience of Tuberculosis may not be the same in other cities or indeed countries, as a result of variations in demographic, treatment regimes and the social context of people at risk. This strategy is congruent with the broad methodological perspectives and approaches to qualitative research that do not specifically value 'generalisability' as a viable or important concept in scientific endeavour(43).

3.7 Search criteria

Two board terms were expressed in the search and then combined to provide results of London studies that explored the barriers, perception, attitudes and knowledge of at risk communities or those being treated for Tuberculosis. The following MESH headings were combined in the following manner:

1. TUBERCULOSIS /TB and REFUGEES = 2668
2. MESH headings for ASYLUM and SEEK* were separately searched = (472)
3. MESH headings for HOMELESS PERSONS were separately searched = 2337 and homeless* = 3340
4. The results from the 'asylum seekers' or 'homelessness' or 'refugee' were combined = 7011
5. These were then combined with the Tuberculosis and refugee search (1) to provide = 235 results

These searches identified the extent of the literature where these terms were present in the title and the abstract of the papers. However, whilst these terms and combinations identified the correct population and 'disease', the search did not provide any literature that directly related to the perceptions, barriers, or cultural or social experience of people experiencing Tuberculosis in London. The following additional search was therefore undertaken:

1. MESH headings for ATTITUDES TO HEALTH = 58240
2. PERCEPTIONS = 16916
3. ANTHROPOLOGY, CULTURAL = 1035
4. SOCIAL and MEANING = 1899
5. EXPLODE-CULTURE = 75567

6. COMMUNICATION BARRIERS = 2579
7. BARRIERS = 19137
8. KNOWLEDGE = 66229
9. These results were all combined to provide evidence that included these terms in the title or the abstract = 59

A further search was conducted to narrow down these two groups of papers to London studies. The following MESH terms were searched:

1. LONDON=0
2. London (title/ab) =4840

This search was then combined with search results from 9 to provide 12 papers in CINAHL databases that related to the subject matter. The same search was repeated in MEDLINE databases and this provided a further 34 results. I reviewed the abstracts of these papers in order to make the final selection. One other paper was identified from an internet search that had not been published in a scientific journal but had been commissioned by the Health Protection Agency in south London. Whilst not published in a peer reviewed format, this paper most closely examined this area of investigation. I will now discuss the results of these searches including my reasons for inclusion and exclusion.

3.8 Final selection of included papers

Only 3 papers were finally identified that provided literature in the London setting, (including the HPA study, published online) and one study conducted in Seattle, USA was also included, making a total of four papers. Reasons for exclusion were studies that did not address the search criteria, service evaluation studies and studies that occurred in populations other than those described in the search criteria. Table 4 identifies the key elements of each of the papers which I shall now discuss in more detail.

Table 4: Selected papers

Authors	Title	Group studied	Methodology	Social context	Main findings	Main recommendations
Shetty N et al 2004	Knowledge attitudes and practices regarding Tuberculosis among immigrants of Somalian ethnic origin in London: a cross sectional study	Somali subjects- multilingual and 'educated'	Quantitative fixed point structured questionnaires	Inner London	Subjects understood TB as infectious disease Poor knowledge of other risk factors Understood TB as 'bio-medical 'disease (men more likely to have this view than women).	Address uncertainties in core TB knowledge
Sebastian MS and Bothamley GH 2000	Tuberculosis preventative therapy; perspectives from a multi-ethnic community	Multi-ethnic groups	Qualitative-structured questionnaire	Inner London	General knowledge of TB was associated with better treatment adherence Symptoms of active TB were generally not recognised	Adherence could be improved by better knowledge of TB and a single daily dose of antibiotics plus more information about the difficulties of six month treatment course

Authors	Title	Group studied	Methodology	Social context	Main findings	Main recommendations
Johnson, A 2006	Beliefs and barriers related to understanding TB amongst vulnerable groups in south east London	Muli-ethnic groups plus some prisoners	Qualitative-focus groups	Inner London	Significant social stigma associated with TB Varying beliefs about the causes of TB including 'the weather' and 'extreme temperature changes'	Address culturally determined barriers to TB identification such as stigma Improve education of health workers Improve knowledge among health workers of cultural practices and beliefs that might influence behaviour
Citrin, D 2006	Somali Tuberculosis cultural profile	Somali subjects only	Qualitative-focus groups	Seattle-USA	Beliefs re cause of TB included punishment for bad deeds, hereditary, sorcery and witchcraft. Profound stigma Centrality of 'religion' to understanding and responding to TB The role and belief in traditional healers	Health providers should increase time spent with patients Patients should be educated regarding the curable nature of TB Discuss social ramifications of disease with patients Treat diagnosis with the same sensitivity as a sexually transmitted condition.

3.9 Results

The selected papers reported knowledge, attitudes and beliefs about Tuberculosis in London settings other than one study that explored these factors in Seattle, USA(44). Table 4 outlines the populations studied, the overall approach, the main findings and recommendations of each of the studies selected. I will now describe the findings of these studies in more detail. One of the London studies focused on the Somali community in an inner city environment(45), another explored these factors within a range of 'at risk' groups with particular reference to preventative therapy (46) and the third study included a mixed ethnic population(47). The most enlightening study explored beliefs and barriers related to understanding TB among vulnerable groups in south east London(47).

The focus on knowledge of symptoms and perceptions of disease was identified as important and discussed in all three papers. Knowledge about disease and disease prevention can potentially influence the ability for individuals to recognise symptoms that may require assessment and treatment(45). Varying degrees of knowledge are present among the groups studied. Poor knowledge and misconceptions about Tuberculosis and basic symptom facts can lead to unnecessary avoidance behaviour, stigmatisation and isolation of those afflicted(45;47). Knowledge about the degree of exposure required to contract Tuberculosis for instance can lead to social avoidance of an infected person and in some cases, deliberate isolation(47). For instance, common perceptions regarding how the disease is transmitted included, spitting in the street, sitting next to someone coughing, sharing crockery and cutlery and cups, kissing someone with TB and sharing clothes and cigarettes(47). In this particular study, the researchers reported that the different groups held various health beliefs about risk factors for Tuberculosis. The Somali group for instance held the belief that the weather was a significant cause of transmission of Tuberculosis, with extreme changes in temperature being identified as important(47). This study also reported a high degree of stigma and negative social connotations associated with a diagnosis of Tuberculosis. Tuberculosis was described by some participants as a 'dirty disease' and rendered those with the condition 'outcasts' from the community(47). Knowledge of symptoms and disease treatment was another important factor identified by Sebastian et al and these researchers identified a correlation between disease

knowledge and treatment adherence, supporting knowledge as an important component to successful treatment(46). Knowledge of disease varied in this area and among a London Somali community a gender specific relationship was suggested. It was found in this study that men were more likely to hold a belief in bio-medicine as a conceptual framework for understanding the disease more so than women(45). The Somali community in general were the most widely studied in relation to health beliefs, knowledge and perception of Tuberculosis but only the two studies identified in this review focused on London communities. Additionally, there were some quality issues with the studies identified in this review. The Sebastian study (46) was rather small including only 24 subjects. Interviews were 'structured' and conducted in English, which in a multi ethnic community may have resulted in the subjects misunderstanding the questions. As I have already discussed the sample size in qualitative research is often small and this is not significant in itself however, the description of the *' interviews'* described by the authors were based upon a highly structured questionnaire that included yes/no and closed item questions. This approach leaves very little room for an inductive analysis in the subject area and one could argue that the method employed was not qualitative at all, although the authors do report inclusion of 5 open ended questions regarding symptoms and transmission which were *'thoroughly explored'* in order to illicit themes from the data, although there was no evidence of how this process was undertaken. Additionally, the interviews were undertaken in clinic prior to the subject's appointment with the doctor and this too may have affected the quality of the interaction as subjects may have been anxious prior to their appointments. Shetty's study was less problematic (45). Their study included only 23 patients but also included two groups of controls (total of 75 subjects). Their study employed a Somali doctor to translate and administer the questionnaire and a cross checking and reverse questioning was employed to ensure consistency of response. Knowledge of Tuberculosis was assessed using a similar approach to the Sebastian group but this study did not describe itself as taking a qualitative approach. Unfortunately, the research report does not say anything about the setting or the timing of the interviews which can be an important factor in influencing subject's response. Additionally, the fact that the interviewer was a doctor may have affected the willingness of subjects to provide favourable answers or ones that they felt would please the doctor, therefore giving rise to responder bias. The authors do readily acknowledge this limitation and discuss other limiting factors

such as difficulty recruiting this group and the subject's unwillingness to provide personal demographic details which resulted in an incomplete data set and an inability to match controls against the index group. Although not explored in their paper, this finding provides an important insight into the challenges of Tuberculosis research and suggests a problematic dynamic between the health providers and their patients that may be significant in treatment adherence.

Johnson's study was by far the most useful as a qualitative investigation into knowledge and beliefs of a London community regarding Tuberculosis. However, this study too posed a number of limitations. These included an inconsistency in the method used, as one group preferred the structured interview approach rather than the focus group approach. The facilitators running the focus group sessions were not of the same ethnic background as those who took part and did not speak the same language as participants. Differences in background and language familiarity may have affected what the subjects were willing to share and moreover, what both the subjects and the facilitators understood. Johnson's group also reported a difficulty in securing the interest and commitment of some of the groups and this he reported was time consuming. This was explained by *'research fatigue'* as many of the invited groups have been the focus of many research projects over the years (47). Although published on the web, I could find no evidence of a peer reviewed publication of Johnson's study, a factor which he reports himself to be problematic, in his review of the literature on the subject. Additionally, there was no detail in his research report that provides an audit trail of how the findings related to the focus group discussions and therefore it was not possible to make any robust judgements on the process of data analysis.

The paucity of London studies demonstrated the lack of an evidence base clinicians possessed around the experience of Tuberculosis for those at risk and highlighted the need for more in depth studies that addressed these important questions taking into account the weaknesses of existing studies. Whilst it is likely that more can be learned from wider assessments of the literature in similar settings, it must be noted that differences in social circumstance, service design and provision can render studies difficult to compare from one part of the world to the next and therefore may not be transferable from one context to the other. This is especially true of qualitative

research where there is an assumption that the concept of generalisablility, taken from traditional scientific and often quantitative frameworks, does not fit the paradigm of interpretive method that focuses on the experience of individual life and social phenomena that are by their nature, unique(43). It is important that the results of qualitative research are understood within the geographical area and the time frame in which the research was undertaken(48). These principles make such research papers difficult to compare. On the other hand, tentative assessment of the literature baring in mind, this potential philosophical conflict can illicit important lessons in method, *'avoiding fruitless approaches, discovering important factors relevant to the topic'* and deciding which questions may be important to ask in the absence of any substantial knowledge or theory in the research area(49). For example, a study in Seattle, USA, published online in 2006 (44), held some resonance with my own experience and the reports of the Somali community in London. I felt therefore that this similarity, despite the difference of context and experience was, in itself an important factor and it was for this reason that I discuss it in this review. The Somali community also has a high level of Tuberculosis notifications within London and Brent specifically(32).

The Seattle study conducted focus group interviews with Somali community members and explored health seeking behaviour, treatment, social meanings and consequences of the illness in recognition of the importance of what the researchers describe as 'cultural' determinants in shaping people's responses to health and illness. Commonly held beliefs surrounding the origins of disease among the Seattle group, included punishment for bad deeds, Tuberculosis as a hereditary disease, sorcery and witchcraft, as well as a bio-medical understanding of contagion. Traditional healers were identified as important first line management strategies for treatment of Tuberculosis and such treatments were administered on the basis of the type and character of the cough, its depth, associated pain and other symptoms(44). Traditional and spiritual treatment was often favoured due to the stigma associated with the disease in Somalia and respondents told stories of how the afflicted were isolated in special huts and treated with traditional medicine, as this allowed a greater degree of privacy and concealment of the condition. Reading specific sections from the Koran was also believed to be powerful medicine in the treatment of Tuberculosis as it was a strongly held belief among this group that the disease is caused solely by God. One

can easily imagine how these perceptions might translate into behaviour and responses to disease in the migrant setting, in this case, a large American city, where it is likely that communities are close- nit and depend upon each other for social support. Stigma was a strong theme in this study and in the London studies and it is understood as an important driver in people's responses to disease. It was noted that in the Seattle study, people with Tuberculosis were *'treated very differently'* in light of their diagnosis and that people were generally afraid to discuss a diagnosis publically(44). Similar themes regarding stigma were reported and described in one of the London studies in particular(47). Although interesting, the Seattle study was not peer reviewed and provided no information on data analysis, little on method and it is therefore difficult to provide a comprehensive critique.

In summary the selected papers provided some insight into social and community life and how perception, knowledge and belief might influence how people behave and the health seeking behaviours people might chose (or avoid) in relation to their diagnosis and treatment. The studies particularly highlight the role of stigma and culture and the affect these factors may have on behaviour as a response to illness and diagnosis. Knowledge is also identified as an important factor as it affects beliefs about Tuberculosis causes and treatment, which in turn can determine how people behave, including health care professionals. However, the knowledge base for understanding these elements is weak with very few studies addressing these problems in London, UK in relation to Tuberculosis. Prior to discussing how the research questions emerged from this literature search, it is important to explore the concepts of stigma and culture a little further, given their apparent significance in the behavioural response to Tuberculosis, within these studies.

3.10 Stigma

Stigma is a socially constructed response to social or personal conditions that are harmful to identity. Sociologically speaking, it is generally understood and explained within the context of social deviance(50). Goffman, in his book *Stigma; notes on the management of spoiled identity* was the first to describe the concept of stigma and the influence that social labelling can have on individual behaviour and the treatment of those who are stigmatised (51). Stigma is defined by its relationship to devalue: 'in which one individual is disqualified from full social acceptance. It can be physical (a

blemish), documentary (a prison sentence) or contextual (bad company), as well as ascribed or achieved'(52). The concept of 'taboo', though closely linked with the idea of stigma remains distinct in its meaning. A subject that is taboo is 'forbidden' or 'unclean' and therefore excluded from daily experience. Frazer first described this concept in the context of Polynesian society. In his seminal work *The Golden Bough,* he described the concept of taboo as the following: 'A prohibition, especially in Polynesia and other south specific Islands, excluding something from use, approach or mention because of its sacred and inviolable nature'(53). He understood this to be very much as something in the imagination of the people he studied and observed *'the danger is not less real because it is imaginary; imagination acts upon man as really as does gravitation and may kill him as certainly as a dose of prussic acid'*(53). The object of taboo is separation in order to prevent the contamination or 'pollution' that is perceived by the social group from the prohibition. Whether this belief is based upon mythology or fact does not undermine its ability to shape behaviour and harm individuals.

3.11 Culture

The combined terms used in the literature review did not provide any enlightening discussion about the role of culture in response to disease, however, it is a subject that is well documented and discussed in the wider health literature and it is important to make explicit the reasons why culture maybe important in defining and articulating disease response in different groups of people. The earliest definition of culture in the health literature and perhaps the most well-known comes from the work of Tylor in 1871 who defined culture as ' *that complex whole that includes knowledge, belief, art, morals, law, custom and any other capabilities and habits acquired by man as a member of society'(54).* In other words, culture is defined as a set of shared systems which people inherit which tell them how to behave, how to experience the world emotionally and how to responds to others and interpret experience(55). People acquire their culture through the process of *en*culturation, where these shared systems and beliefs are learned and transferred by growing up in a particular society(55). Cultures exist within all societies and share similarities such as the components of culture that define how society is described, broken up, categorized and understood(55). For instance, most cultures define systems within society that

describe social stratification, the roles of men and women, as well as defining what is 'normal', 'abnormal' or deviant for example. Behaviour, belief, language and religion, how people dress and what they eat all have their roots in culture. Cultural background therefore has the potential to deeply influence how a person thinks and behaves and this includes response to illness, misfortune and suffering(55). In Rangan and Uplekar's paper on socio-cultural dimensions of Tuberculosis control, they describe how these factors affected the life of one patient in Western India(56). The story describes how Sharda, a young woman, suffered a multitude of delays to diagnosis and treatment of her Tuberculosis due to the inability of her family to accept the diagnosis, the fear of her condition becoming known in her village, and the subsequent secrecy and concealment of the diagnosis that was maintained in order to preserve her place and status in society. Eventually Sharda had to attend a clinic and face a barrage of *'barbed remarks'* from her neighbours as her secret was revealed(56). She was eventually abandoned by her husband and his family and her husband even remarried. The story illustrates how 'cultural' belief and social context can determine responses to illness and highlights the importance of this question in exploring perceptions of the disease in any setting where it may present a problem. Typically however, Rangan and Uplekar's paper, does not define what they conceive to be the 'cultural' element of this experience and this does highlight the difficulty in isolating pure cultural elements from any human experience(55).

The literature review provided little evidence in relation to knowledge, the social meaning, and perceptions of disease and how culture among different groups in London might influence treatment outcomes or become barriers to successful treatment although there were plenty of examples of how these factors may influence the Tuberculosis story in other settings and countries (57-59). This is despite the recognition of their importance(60). There were no studies that focused specifically on North London, an area of the city that was experiencing particularly high prevalence rates and consequently very little understanding of the specific problems experienced by the Brent community. There was also a paucity of evidence that explored these factors from the health professionals point of view and whilst it is true that the communities at risk are an obvious focus of enquiry in relation to these factors, it is also important to consider the health professionals experience in providing the services and whether there are limitations and barriers from a service

perspective. I wondered how much these social and cultural factors were reflected in the London context and whether they were shared by the various groups identified at risk within the Brent community.

3.12 Research questions

The focus of the research aimed to explore these factors.ie, the community reaction to Tuberculosis, as well as knowledge of disease from within the community, whether specific cultural beliefs influenced perceptions and reactions to disease and how these factors might influence health seeking behaviour among these groups. The experience of health providers was also an area for investigation given that successful treatment is often dependent upon good relationships between health providers and service users(61). The research questions identified for this study were as follows:

1. How might community experience influence disease prevalence of TB among refugees, asylum seekers and homeless people in Brent (high risk groups)?
2. Are there cultural and social factors in different refugee communities and do these affect people's willingness to be treated or seek help?
3. What are the barriers that may affect the uptake and service delivery to asylum seekers, refugees and homeless people?
4. What are the institutional gaps in prevention, detection, notification, diagnosis, treatment and follow up?
5. What is the knowledge level regarding Tuberculosis among these groups?

3.13 Deciding a methodological approach

The selection of research methods for any line of enquiry should usually reflect the nature of the problem under investigation(62).Quantitative research approaches generally have their roots in the Positivist experimental sciences and are concerned with 'casual determination, prediction, manipulation and generalisation'(63). Qualitative methods are interpretative and seek to illuminate, *'understand and extrapolate findings to similar situations'* (63) often building knowledge and theory where little knowledge exists. Critics of this approach have asserted that the lack of generalisability that the work generates reflects a weakness in its power to advance knowledge(64). However, the intention of qualitative research is to gain access to the

experience of others and to describe often complex social phenomena(65) rather than to measure and quantify phenomena using statistical means, that claim generalisability(63). The purpose of qualitative research is to understand the world as it is lived, through the eyes of others and thus provide a rich description of meaning and context of lived phenomena. The nature of life and experience is such that individual perspectives are inevitable and may not be generalisable to the population at large, yet it is difficult to deny that the individual perspective should not be central to the experience of health and medicine and indeed, this is increasingly being recognised(64). There is therefore, a legitimate requirement to understand experience at a more individual level and to understand how social, cultural and even political contexts can shape perceptions and expectations of health and the possibility of wellness. This is an especially important endeavour where the communities that are affected by disease are socially vulnerable and where the influences of the political, cultural and historical factors are powerful forces that shape opinion and behaviour(66).

The *'images of reality'* obtained from qualitative enquiry can elucidate understanding regarding behaviour(67). In terms of health choices and health seeking behaviour, the knowledge gained can inform health service design. They too can be extremely useful in approaching questions about human experience and its meaning(62). This relative 'truth' as opposed to the ambition towards 'absolute truth' in quantitative research provides part of the strength of qualitative work, as it can often provide an inductive base for building theory rather than testing it(68). It has to be said however, that gaining access to another's life experience is rich with philosophical complexities. For instance, is it really possible to unravel the 'essence' of experience as it is perceived by another in the way in which some qualitative researchers claim? For example, in some schools of phenomenology, the intention of research is to '*secure absolute insights into the what, or essence, of whatever is given intuitively in experience'*(69).This *'essence'* of experience is viewed and interpreted through ontological and epistemological perspectives that define the nature of being and the nature of knowledge, to give meaning and structure to human experience(69). One of the challenges underlying this methodological approach is to know when such a state of understanding has been attained, and to be able to demonstrate the authenticity of the presented results(70). This rather nebulous ambition has given rise to criticism

regarding qualitative method in general and its ability to provide valid and reliable results. Some quantitative scientist would propose that use of such methods produces work that is *'merely an assembly of anecdote and personal impressions, strongly subject to researcher bias'*(64). Others would argue however, that reliability and validity are not the point and that these concepts are not congruent with the philosophical basis of qualitative research(71;72). These concepts relate to accuracy, relevance and reliability of measurement (validity) and the *'consistency and constancy'* of a measuring instrument(73) whereas, in qualitative research, it has been argued that effort should be more directed towards demonstrating the *'dependability'* and *'credibility'* of the work in order to show the' *trustworthiness'* of the research(74). In other words, how closely does the work reflect the experience of the study participants?

Regardless of these methodological challenges, qualitative methods provide a valuable tool to explore and explain human experience. But this understanding has the potential to be limited by our own experience as researchers and professionals (as well as enhanced by it), as well as by our language and the understanding of linguistic concepts(75). How far the world is shaped by the language we speak, and to what extent variations in language limit our comprehension of it, are important considerations when conducting research that involves different languages(76). It is important to acknowledge that the linguistic gap, no matter how well one addresses this in method, may still exist in meaning in the final analysis.

Qualitative researchers understand these concerns and acknowledge that language, history, culture and thought have an impact upon the observer, the process and the finished product of qualitative research. Researchers themselves may have influence upon the process of research and the interpretation of the phenomena being studied. It is not possible to entirely suspend one's own consciousness, history, opinion and so forth, in order to achieve an entirely objective analysis of another's experience but, it is possible to make these facts explicit in doing the work in order that the 'trustworthiness' and the 'credibility' of the analysis can be judged by others(63;74). The process by which these assumptions, experiences and expectations are made explicit is an important component of rigor in qualitative method and is known as reflexivity(77). It is based upon the contemporary position in the philosophy of

science that there is no such thing as a neutral observer (67;78). It further supports the notion that the observer's view '*is always limited and determines what can be seen'* rather than what might be available to view(78) .There is no way out of this argument, in that scientists are human and are therefore fallible. However, qualitative research does acknowledge that the identity of the observer and the nature of observation are almost as important as those being observed. These methodological concerns will be explored as they become relevant to this thesis.

If we consider and bring together some of the fundamental differences discussed here between quantitative and qualitative approaches, it becomes clear to see that the questions posed by this research lean more fittingly towards a qualitative framework in the questions that deal with experience, the social and cultural elements, but also suggest that some quantitative exploration would be legitimately employed, to measure knowledge, for example. Table 5 outlines the main differences from a variety of important defining characteristics between quantitative and qualitative research. This table has been loosely adapted from (76) and brings together the concepts discussed in this section.

Table 5: Defining characteristics and differences between quantitative and qualitative research

Characteristic	**Quantitative Positivism**	**Qualitative Interpretivism**
Broad philosophical basis	Assumes one objective reality Seeks causal relationships Ontological basis-human beings are reduced to systems/organs/tissues/cells. Everything can be measured	Accepts multiple realities Assumes social reality is 'constructed' not discovered Ontological basis-'being' is dependent on social and cultural and historical context
Main objective	Verification	Concept and theory development
Types of questions posed	How often? How many? Which is better?	Why? What?
Setting	Usually experimental	Natural setting
Variables	Often controlled and manipulated	Often not known
Study population	Numerous, large and heterogeneous	Few and small and often specific
Approach	Deductive /reductionalist	Inductive/holistic

Characteristic	Quantitative Positivism	Qualitative Interpretivism
Analysis	Statistical/mathematical	Interpretative
Results	Hypothesis/theory testing	Hypothesis/theory generation
Researcher	Objective and distant	Involved and reflexive
Presentation of results	Focus on data and prediction	Focus on narrative, 'stories' and description

3.14 Research questions, approach and method selection

Having identified the research questions following the literature review and identified the gaps in the evidence it was clear that each question contained elements of both quantitative and qualitative method and I felt it was important to reflect the mixed philosophical elements of each in the appropriate selection of method. I carefully considered the focus and the nature of each question against the above broad criteria in order to ensure a fitting research approach to each element. The results of these considerations are as follows:

1. How might community experience influence disease prevalence of TB among refugees, asylum seekers and homeless people in Brent (high risk groups)?
   Qualitative approach indicated: asks question relating to experience

2. Are there cultural and social factors in different refugee communities and do these affect people's willingness to be treated or seek help?
   Qualitative approach indicated: asks questions relating to experience and how this might influence health choices

3. What are the barriers that may affect the uptake and service delivery to asylum seekers, refugees and homeless people?
   Qualitative approach indicated: Little is known about the barriers from either the point of view of service users or potential service users or from providers' perspective.

4. What are the institutional gaps in prevention, detection, notification, diagnosis, treatment and follow up?
   Qualitative approach indicated: Little is known about institutional gaps in

relation to these groups of people from either the provider or the service user perspective.

5. What is the knowledge level regarding Tuberculosis among these groups? Quantitative approach indicated: Knowledge about disease symptoms and treatment are known *a priori*, therefore can be measured.

Further to the iteration of the questions and the decided approach some of the questions were more appropriately directed towards members of the community whilst others were clearly directed towards the health professionals (providers).

Questions 1 and 2 were more directed towards to community groups as they largely ask questions relating to the experience of community members whilst the latter questions were more concerned with health professionals' experience, questions 4 and 5. Question 3 was answered using an amalgam of responses from both perspectives.

3.15 Method selection

There were a number of challenges involved in choosing the appropriate methods to gather data from within the chosen sample to answer the above questions. The methods needed to be practical, within the limited recourses available and take into account any language difficulties and differences. Two approaches were selected using a combination of both quantitative and qualitative data gathering tools in order to allow some triangulation of the information gathered and also to allow measurements of some of the more quantitative elements. I also needed to consider my relationship to the Brent community and possibilities of gaining access to the field and how my presence might affect the quality of the data gathered. Given the variety of ethnic and cultural groups within Brent, I needed to select a method that could capture the many perspectives in relation to the research questions. A combination of focus group sessions and data obtained from questionnaires was finally selected to gather the data. The reasons for this will now be explained.

3.16 Focus group research: why do it?

Focus group research allows researchers to engage a small number of people who may have views on a 'focused' topic or a specific set of issues(79). They are particularly

helpful to allow discussion regarding feelings, perceptions, opinions and thoughts(80) Additionally, they are fast, economical and efficient at obtaining information from multiple participants(80). As participants usually share the phenomena in question, there is often a feeling of belonging to the group which encourages a sense of cohesion and safety enabling participants to express their views freely(80). One particular advantage of the focus group method is the element of group dynamics which are inherent in this type of structured group discussion and it is argued by some, that this gives rise to a richer and deeper description of the phenomena being studied(81). As well as illuminating shared experience about a particular topic, focus groups can be useful in teasing out the conflicting views held by participants and the differences in perspective(82).There are some challenges however in conducting this type of interview. The role of the moderator is crucial and a lot depends on the skill of the moderator and the relationship he or she has with the participants as this allows them to feel relaxed(82) . There is also a risk of moderator bias as with any qualitative method, the moderator could be more inclined to lead the discussion according to their own views or perhaps miss out important leads in the discussion(83). It is for these reasons that the moderators of the groups should be very well prepared and conversant with the subject being discussed(82;83). Since the strength of focus group research can be in the dynamics that emerge from the group, so too can be its weakness, in that shy and retiring participants who have valid contributions can be dominated by more forceful and dominant members(83). Part of the skill of the moderator therefore lies in his/her ability to manage these group dynamics. Baring these factors in mind and given the differences in culture, race and spoken language between myself and the people of Brent that would be asked to take part, it became evident that I would not be well placed to take on the moderator role. I would not be in a position to develop rapport and trust with the people targeted. The literature reports the importance of these social factors and the congruence between the racial and social profile of the researcher with the targeted groups, as it can be a significant factor influencing disclosure(84). Indeed, I did not speak any other language fluently other than English. Additionally, it became evident that the refugee groups that agreed to take part were in themselves diverse, originating from many parts of the world and some were unable to speak English at all. This point will be addressed in the next section as well as the strategies that were employed to overcome some of these barriers.

3.17 Methodological concerns of focus groups

There were two main methodological challenges in deciding how and where to run the focus groups. Language was the primary concern, as many people in Brent do not have English as a first language and, if they do speak English, there may be concepts and feelings that are not easily translatable from their own language into English(85). It was crucial, in attempting to understand the community perception of Tuberculosis in differing community groups, that a conceptual equivalence from one language to another was attempted, although this aspiration is noted as difficult to achieve(86;87). In order to mitigate the language problem, and differences in background and racial profiles, volunteers were recruited from within the target communities of the same ethnic background, and who spoke the same language as the target groups as has been suggested in the previous section(84) . It was also important that the group leaders running the discussions were trusted members of the target community as discussed earlier. As a result, and through the links that Dr Mahmoud had within the Brent community, the focus group leads were selected from local community refugee groups and the sessions were held within these organisations. There were some weaknesses in this approach however; the volunteers were not experienced in leading focus group discussions, nor did any have particular knowledge of qualitative research methods. To mitigate this as much as possible, I led a teaching day for all the selected group leaders on focus group method, the aims of the research and the proposed format of the focus group sessions.

3.18 Sampling strategy and selection of participating groups

A convenience sampling strategy was employed to select the groups which reflected the links that I had established with the Brent community. Dr Mahmoud, at the time was employed by the Brent refugee forum and the groups that were targeted to take part in this research were all members of that organisation. It was important to reflect both the population of Brent in terms of the refugee population and also those groups that have been described as being ‘high risk’. These included African groups, homeless groups and those with HIV and AIDS. The following groups gave agreement to take part and in each of them, volunteers, agreed to act as the focus group moderators. The refugee organisations who agreed to take part are listed below:

1. Somali Women Group: moderated by CK Consultancy Group
2. Somali Men Group: moderated by Refugee Links and Training Agency, working in partnership with Brent Refugee Forum
3. Tamil Group: moderated by Tamil Refugee Action Group
4. African French Speaking Group: moderated by Nile Scope Vocational Training
5. African Swahili Speaking Group: moderated by Nile Scope Vocational Training
6. HIV/AIDS Group: moderated by Innovative Vision Organisation
7. Young People group: moderated by The African Child
8. Homeless Family Group: moderated by the Homeless Families Group
9. Single Homeless Group: moderated by Cricklewood Home Concern
10. Afghan Group: moderated by Afghan Association of London

Additional to the community groups one focus group of GPs was included and a specialist TB nurse group.

Figure 4 and Figure 5 show the participating groups, excluding the health professional groups and the ethnic distribution of the sample.

Figure 4: Participating groups and communities

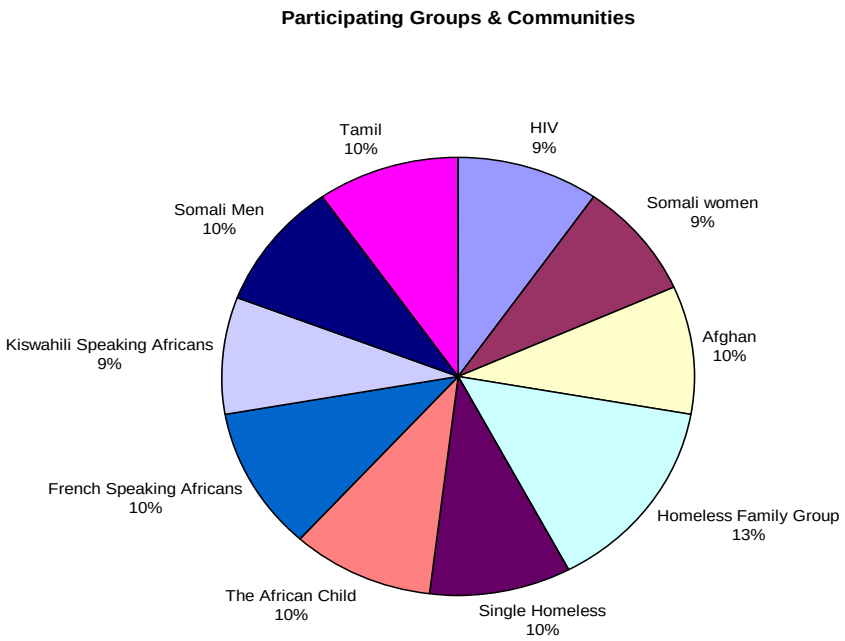
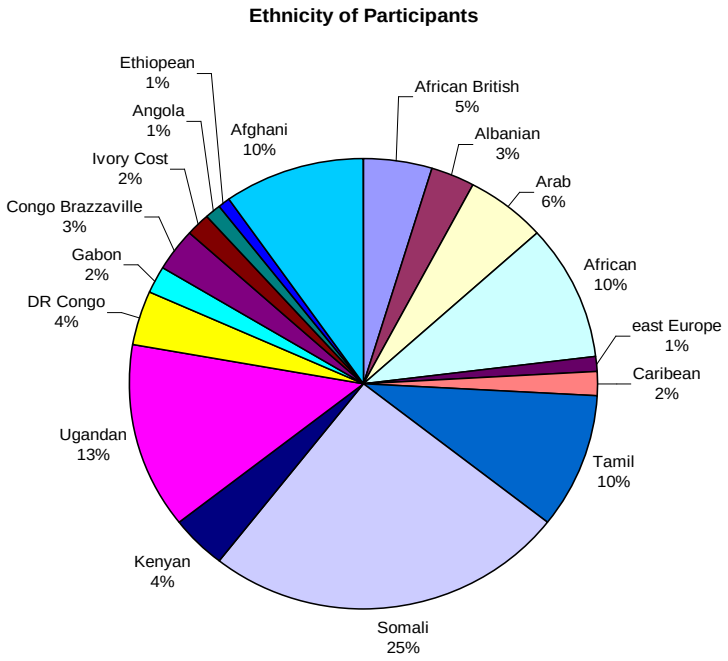


Figure 5: Ethnic distribution of those who took part



The groups included were thought to be especially at high risk from Tuberculosis for the reasons already discussed in the literature review. Unfortunately, we were unable to access any groups originating from the Indian sub-continent, which form a large proportion of the Brent population and also feature highly in the Tuberculosis notification numbers for Brent and London(30;32). The heavy emphasis on African groups reflected the particular risk associated for those people originating from those African countries with a heavy disease burden(32). Two Somali focus groups took place. One male and one female group were held separately. The separation of the male and female Somali groups was decided upon as a result of consultation with the Somali group leader, who felt that because of cultural, religious and social reasons, both women and men would feel more comfortable and less inhibited, if the groups were separated by gender. There may have been other social and cultural elements within the dynamics of the groups' make-up that could potentially have affected the outcome and the quality of the interview that could not so easily be accounted for. It was important to ensure that wherever possible potential participants would feel comfortable with each other(82). Homogeneity, in terms of gender, race, and social background is generally encouraged to facilitate the degree of trust and openness required for successful participation(80;82). In some cases, the ideal mix of

participants is difficult to predict and some elements of group dynamics could potentially have impeded contribution from some members. For example, the presence of particularly dominant or shy members is difficult to account for and how this dynamic is managed in reality is often dependent upon the skill of the moderator(85). Given the unpredictable possibilities of group dynamics, a questionnaire was also included that tested basic knowledge of Tuberculosis symptoms, any previous experience of Tuberculosis and questions relating to perceptions of disease. Data gathering using the questionnaire was conducted face to face and in private. These results were triangulated, where relevant and where possible with the outcomes of the focus group sessions and shall be discussed in the results section. The inclusion of the questionnaire, its development and design will also be addressed later in the thesis.

3.19 Sample size

There appears to be general agreement in the literature that the size of a focus group should be relatively small, ideally between 6-10 participants in each session(82). However, some recommend much smaller groups of 5 or 6(88). The target number for this project was approximately 10 participants per group. The number of groups advocated to provide rich data to inform any area under investigation is approximately 4-6 groups per topic(88). The relatively large number included in this research reflected the diversity of the population targeted and the inclusion of both health professionals and community members.

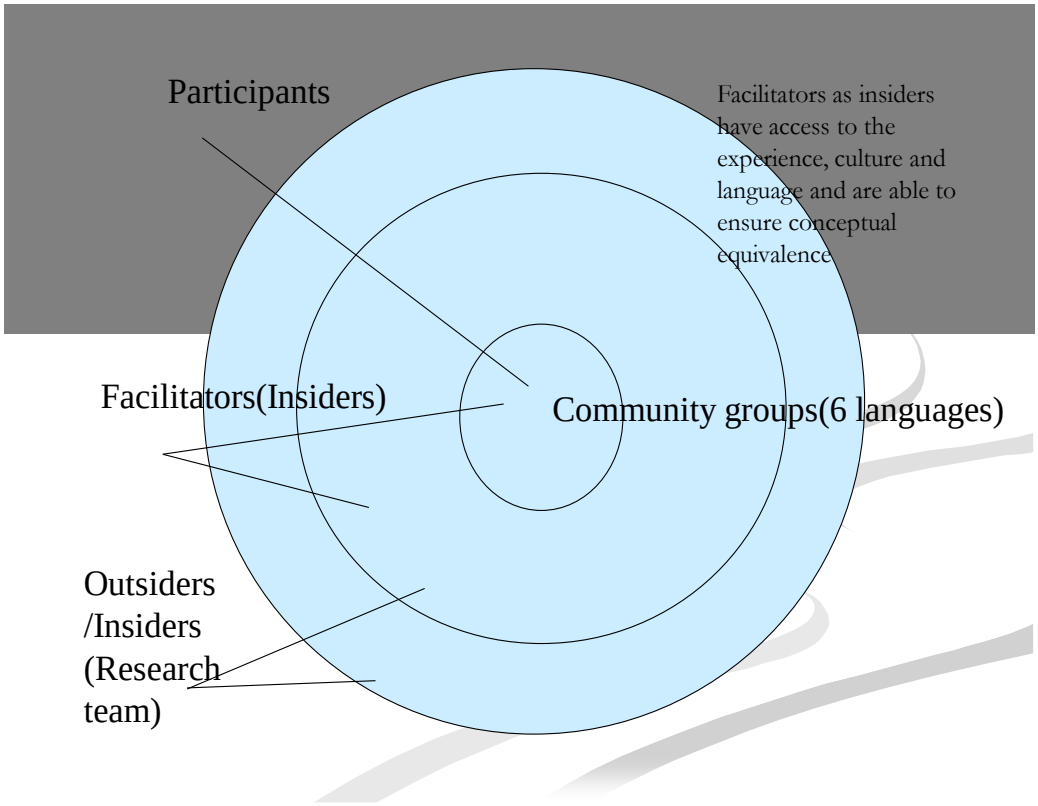
3.20 Researcher Positioning: Primary considerations

The research team consisted of Dr Amna Mahmoud of the Brent Refugee Forum, Dr Sufi from the Health Protection Agency, Ms Kultrum-Rivers, an independent research consultant, myself and Professor Malone-Lee of UCL. My role in this study was as study supervisor and co-investigator. Deciding who would undertake the work 'in the field' was crucial to its success. In terms of the Brent population we (the investigators at UCL) were outsiders on many counts, firstly by virtue of our cultural background, language, religion and our professional perspectives. Additionally, our professional identities may have acted as barriers to participants' willingness to tell us their stories(88). Moreover, I did not speak the various languages used within the target

communities and as the refugee community consisted of many newcomers to London, I assumed that English was not a first language for most. This language gap posed a specific methodological challenge in my ability to obtain high quality data for in depth qualitative analysis and to allow meaningful interpretation of the data, a theme which is explored in detail later on in this work. Dr Mahmoud, who acted as the bridging investigator, was well placed within the community and well respected, and given her position as 'an insider', was able to recruit the groups and the volunteers from each section of the Brent community to undertake the data gathering for the study. The positioning of the research team had to take into account the relationships of the investigators to the target groups, how we would be perceived and whether differences in ethnic origins, culture, gender and possibly education may have served to alienate the participants from the team as well as bias our ability to understand what was discussed. This is a recognised problem in qualitative research in general and in focus group research and particular attention should be given to addressing such issues(88). The moderators that led the focus group discussions were employed by the agencies for which they worked and were respected members of their community. They therefore had access to the language, culture and history of that particular group. One disadvantage of this approach however, is the possibility of the 'closeness' of the moderator to the target group to blur the boundaries between the roles of moderator and participant(84). I am unsure whether this was a factor in the running of the sessions as I was not present at any of them. The investigators; myself, Dr Mahmoud and Ms Kultrum Rivers positioned ourselves outside the target communities and took no part in the data gathering process of the community groups. I led the education for the moderators, (discussed later) and supervised the method development, ethics application, protocol development and analysis. Later, I interviewed the specialist nurses as an 'insider' of their group and Dr Mahmoud led the GP group. The positioning of the research team in relation to the communities is shown in Figure 6. The importance of the 'insider position' of bilingual or multilingual moderators is also crucial in ensuring conceptual equivalence in meaning of one concept to another from one language to another. This study provided me with a starting point to gain understanding about the social and cultural context of Tuberculosis in one of London's most affected boroughs. It provided an opportunity to ask questions that were significant in terms of the health beliefs of high risk groups, and to assess their knowledge, perceptions and whether cultural positions and beliefs influenced

behaviour and the resultant relationships between the community and the health services that provide Tuberculosis support.

Figure 6: Researcher positioning and relationship to the field



3.21 Number of focus groups-rationale

Following agreement regarding the positioning of investigators in the field, and given that the ethnic diversity of the communities in Brent was extensive, as were the selected groups; the focus group sessions were conducted in the native language of the participants. The culture, belief, experience and language of one group could not necessarily be merged with another as each possessed unique experience, language, culture and so on. They were not one homogenous group. As each group was treated individually, I was able to achieve a significantly larger dataset than is usual for qualitative research which could be viewed as both strength and a weakness. On one hand, a rich description of the phenomena in question was achieved that reflected the broad view of community perception regarding Tuberculosis. On the other hand, there were clearly differences between groups that were captured in the focus group sessions, as the data gathering was not pursued to the point of *'data saturation'* within each separate ethnic group(89). I.e., the continuation of data collection, until *'a clear*

pattern emerges and subsequent groups produce only repetitious information'(82;90). Since the intention of this study was to obtain the broad community view regarding Tuberculosis and not an in- depth investigation of individual ethnic group's perceptions; it was only practicable to conduct one session per group rather than more than one, that may have elicited data sets that were closer to saturation. Whilst I was able to maintain homogeneity in terms of the participants in the groups, I was not able to achieve this in the final data sets.

3.22 Preparation of the focus group moderators

The group moderators, although highly motivated to undertake the focus group sessions had no formal training of conducting research or running focus groups. Given the importance of the moderator role, some formal preparation is strongly advocated(82;83;90), though some authors state that a degree of naiveté can be advantageous(88). All agree however, that some degree of facilitation skill is required.

The volunteers were invited to the Brent refugee forum for a day's training session, led by myself. The training consisted of a presentation of the research objectives, followed by an educational presentation that outlined some theoretical elements of running the focus group sessions and some tips and hints on listening, keeping people talking and exploring and probing significant points(83;88). It is also advocated that the moderators are in possession of a structured focus group schedule that asks open questions to encourage participation from the participants. The questions and questionnaire and study procedure was explained. The afternoon session consisted of a workshop, where I provided some hypothetical focus groups questions, and encouraged the moderators to role play how they might approach asking the questions. I then asked members of the group to take on specific roles, such as a very dominant member, or a member who seems reluctant to contribute and discussed ways in which people could be encouraged to contribute. I provided useful prompts for them, such as standard questions they could use to delve deeper into an interesting matter, for example, 'so and so has just said something really interesting. Does anyone else feel that way?' or 'what do some of you think about what has just been said'. I explained the importance of the setting, ensuring that it was quiet and convivial(88;90). Some moderators had planned to provide snacks and crèche

facilities to encourage participation and this was particularly important for some of the African women, who would find it difficult to attend with their children in tow.

3.23 Questionnaire design and topic selection

Two data gathering instruments were developed to answer the research questions. A questionnaire assessing the respondent's knowledge of Tuberculosis was constructed, and included basic questions about its causes, transmission, and common misconceptions about disease as well as respondent demographics (Appendix 2). The misconceptions about the disease were derived from reports in the literature. For instance, it is sometimes thought that Tuberculosis can be a hereditary disease or can be spread from one person to another through incidental contact such as shaking hands or sharing plates and cups(44). I have already discussed how potentially this belief may cause people to be unnecessarily isolated and feel stigmatised. I also had to consider that taking part in the research was a health opportunity for the participants, given that access to health care is often described as a problem for refugee communities(33). Although we were not targeting people with Tuberculosis and given the high prevalence of Tuberculosis in Brent, I considered it ethical practice, as a registered nurse to use the research as an opportunity for screening and potential case identification if any clinical suspicion arose. I therefore included some questions that would identify important risk factors, such as cough, night sweats and weight loss, vaccination history, and previous history of tubercular disease and treatment completion(91). If participants reported having any prior tubercular disease, they were asked to report any delays to diagnosis and treatment they may have experienced. These questions were included on the questionnaire, as participants may not have felt comfortable reporting their own prior experience with Tuberculosis in a group setting, given the stigma associated with the condition. The questionnaire was conducted face to face with the moderator and in private. Questions regarding treatment delays included; 'how long after your first symptom did you consult a doctor? And, 'if there was any delay in seeking advice, what reasons can you give for the delay?' (Appendix 2, questions 26 and 27). Given the concern over referral times and the London target set by the Stop TB London group and the quality metrics(41;60), a question was also included about referral times to the chest clinic (question 29). Additionally, a section on 'reaction to diagnosis' and the social impact of TB which asked whether factors

such as social life, relationships and work had been affected by the diagnosis. The construction of the knowledge measurement section of the questionnaire will be discussed later.

3.24 Focus group schedule development: assessing perceptions and barriers

As well as obtaining information that related to participants knowledge I also wanted to identify how the community groups perceived and talked about Tuberculosis and whether such perceptions could constitute barriers to successful treatment and case identification. The focus group schedule (Appendix 3) was a 9 item schedule of open ended questions to encourage active discussion. It was designed to generate data and understanding to answer research questions 1 and 2: *how might community experience influence disease prevalence of TB among refugees, asylum seekers and homeless people in Brent? And: Are there cultural and social factors in different refugee communities and do these affect people's willingness to be treated or seek help?*

Community experience and cultural and social factors and perceptions were elicited by points 4 and 5 in the schedule: *Is there any fear about TB in your community?*

And: *If there is, how is it expressed and talked about?* And item 7*: How does your community respond to TB socially? Is it seen as a negative thing?* The participants were then asked to talk about any negative connotations and perceptions in relation to their own community experience and finally were asked what they themselves would do if they suspected that they had TB: *What would you do, if you suspected that you had TB?*

Given that Tuberculosis is a stigmatised condition and participants may not have felt comfortable disclosing their personal experience; an item was added specifically to encourage discussion around that point but was phrased in such a way as to be indirect. This provided an opportunity for participants to discuss their own experience or that of someone they knew. Therefore the following item was included: *Do you know of anyone who has had TB? What was it like for them?*

3.25 Health professional schedule

The health professionals of course, provided the other half of the story. In terms of assessing the barriers to successful tuberculosis management, the health professional view is obviously important. Adequate skills and knowledge of health professionals in relation to specific cultural needs of different groups promotes culturally competent and individualised patient care(92).Very little research however, has focused specifically on the needs of health professionals in relation to Tuberculosis. The schedule for the nurses and the doctors were therefore designed to encourage discussion in relation to cultural issues and whether they felt themselves, unprepared for, or lacking specifically in skills that would promote more confidence and more sensitive management of refugee and homeless groups. The schedules differed slightly in that the role of the nurses and doctors are quite different in the management of Tuberculosis. The nurses' role is more focused on administration of medicines and supporting the patient and the family through the course of treatment. Therefore, questions were asked in relation to these factors such as: *do you think you have the skills and knowledge and resources to follow-up a TB patient in the community setting?* And: *are you confident in dealing with cultural issues?* Furthermore, the nurses were asked to elaborate on any examples of 'cultural challenges'. The doctors were asked specific questions in relation to diagnosis of Tuberculosis, their confidence in dealing with 'cultural issues' and factors that they felt might inhibit (present a barrier to) successful case finding and management. Both groups were asked about immigration regulation and whether a refugees' immigration status might affect how they approach patients. Both doctors and nurses were also asked to report specific problems associated with treating homeless patients.

3.26 Ethical considerations

As part of the questionnaire we included some questions to assess whether those taking part were currently experiencing any symptoms that could in themselves raise clinical suspicion about the presence of Tuberculosis, such as cough, night sweats and weight loss. If symptoms were found, these would be picked up in the analysis by myself and we arranged that I would identify these cases for the volunteers to go back to the respondent and encourage them to visit their GP. The study was approved by the Brent research ethics committee (Appendix 4). One participant from one of the

focus groups reported a lump in their neck. The participant was advised to visit his GP and was subsequently diagnosed with lymphatic Tuberculosis.

3.27 Recruitment

Once the group leaders had been recruited from refugee community organisations and the training session had been completed, each leader organised their own sessions within the target communities. The group leaders helped recruit individuals who were willing to share their experience and views on Tuberculosis, through their contacts and networks.

Ten community focus groups and interviews in the target communities took place. One group of General Practitioners (GPs) also took part and one specialist nurse group and one in- depth interview with a TB nurse specialist. Consent from participants to take part in the study was obtained by the focus group moderators prior to the start of the sessions.

Information leaflets were produced and distributed to the communities in the appropriate language. These were translated from the English versions to the language of the target groups by the group moderators. All the group moderators had a high standard of spoken and written English.

3.28 Focus group participants

Each group consisted of 8-15 people and lasted at least an hour. The knowledge questionnaires were completed by each participant prior to the discussion, to ensure that opportunity was given to participants to express their views, which otherwise could have been difficult to express during the general discussion. The sessions were tape recorded and transcribed verbatim by the facilitators in the original spoken language of the groups. The transcripts were fed back to those who took part in the sessions before they were translated into English by the facilitators for analysis by the researchers. The total dataset consisted of transcripts in six languages prior to their translation into English.

One focus group of 11 General Practitioners (GPs) took place. I originally planned to interview some patients, but discovered that the recruitment of such people was

difficult because of their reluctance and so we did not accomplish this element. Health professionals were asked about their experience treating TB patients, and the challenges affecting treatment success as already discussed.

3.29 Analytical framework: ensuring reliability and validity

Earlier, I discussed the main differences between quantitative and qualitative approaches and touched upon important scientific determinants of quality, that some have argued are not compatible with qualitative research(93). Reliability and validity are important concepts to be satisfied in any research in order to provide evidence of quality. But these terms are based largely upon philosophical assumptions that are more congruent with the experimental sciences(74). For example, the term 'reliability' is associated with the concept of repeatability and consistency of an instrument and can be tested by its ability to remain stable and provide the same results irrespective of different users and different time-frames(94). The validity of any given instrument determines whether it measures what it reports to measure, i.e., whether the means of measurement are accurate(63). The difficulty in applying these terms to the assessment of qualitative research is inherent in their incompatibility with both the intention and approach of qualitative research. The requirement for instance to 'replicate' a result is not necessarily desirable because the findings are very particular to a specific time, place and experience and will not necessarily give the same result if repeated(63). Similarly, in the context of validity, the intention of qualitative research is not to produce consistent results so much as to accurately describe the experience of phenomena under study(63). In quantitative research for example, the terms used in a research instrument such as a questionnaire have the potential to mean different things to different people and therefore may not measure consistently the same thing(95). One way to overcome this would be to test the instrument by rephrasing the question; i.e., ask the same question in a different way. However, the difficulty of applying this concept to qualitative research is that if we adopt the same strategy, rephrasing the question could easily constitute 'asking a different question'(95). Despite these challenges, it is widely recognised that demonstration of these concepts in some form remains vital in qualitative research in order to avoid the *'methodological anarchy'* that may arise in the absence of appropriate frameworks(70).

As a result of these philosophical problems, alternative frameworks have been suggested that provide a better fit for evaluating quality of studies and guiding analysis. Among the most widely used is Guba's constructs for determining 'trustworthiness' in qualitative research(74;93). In this study, these constructs were employed to guide the 'rigour' of the design, analysis and findings of the study. That is, the extent to which the research results accurately represented the experience of the study participants(96). Guba identifies four stages in this process. Strategies of how I ensured adherence to these criteria and areas where there may have been weaknesses in the design, data collection and analysis are outlined in Table 6 and will be discussed in more depth later in the thesis. The criteria are as follows(48):

a) Credibility: ensuring a 'true' picture of the phenomenon is presented (corresponds to the concept of internal validity)

b) Transferability: ensure enough detail is provided so that the reader can decide whether the research environment is similar to another situation, to which the findings can justifiably be applied (relates to external validity-generalisability)

c) Dependability: although difficult to repeat qualitative work exactly, this provides sufficient detail in order that another researcher could repeat the study in another setting if desired (corresponds to reliability)

d) Confirmability: ensure that it is clear how the findings that emerged from the data emerged (corresponds to objectivity).

Table 6: Strategies for supporting trustworthiness of the data

Quality criteria	Strategy element	Strategy employed
Credibility	The adoption of well-established methods in the field	Focus groups Open questioning
	The development of an early familiarity with the culture of participating groups	Relationship established with the Brent refugee forum; gate keeper to the target groups
	Random sampling-proposed in qualitative work as a strategy to avoid researcher bias(97)	Researcher positioning ensured that the selection of invited participants came from the community group leaders and not the researchers. Participants were invited to take part through posters and flyers rather than cherry picked.
	Triangulation(74)	Different methods were combined in order to gather data regarding knowledge of Tuberculosis. This was then compared with the focus group schedules to validate knowledge reports in the groups. Inclusion of the professional groups also provided additional triangulation across different types of groups
	Tactics to help inform honesty of respondents	Inclusion in the focus groups was voluntary. Group moderators already had good relationships with their community groups. Participants were given assurances that they could withdraw at any time and that they would not be individually identified(48).
	Iterative questioning (ensuring honest responses through rephrasing of questions in another way)	The knowledge questionnaire provided more objective information regarding, knowledge and this was complimented by questions included in the groups focus group schedule: 'what do you think causes TB'. There was no real possibility of false accounts being given to the other elements.
	Frequent debriefing sessions	Bridging investigator provided support to the group moderators, although there were no formal meetings between them.
	Peer scrutiny of the research project	The project proposal was peer reviewed by a senior chest physician.
	Reflective commentary from the researcher	Represents a weakness in the design, as the focus group moderators did not provide field notes or reflective commentary about their sessions.
	Background, qualifications and experience of the investigators	I had some experience and training in social research and qualified RGN. Dr Mahmoud was a physician(not registered in UK) Group moderators had little training and experience in running focus groups
	Member checks	Transcripts were validated by the groups Themes were validated by the groups
	Thick description of the phenomena under scrutiny(74)	Examples of the participants' views and opinions have been provided in the text to back up inferences and themes proposed in the findings of this study.
	Examination of previous research findings(98)	Literature review provides analysis of similar and relevant work and research is discussed in the findings that support or refute the work of others

Quality criteria	Strategy element	Strategy employed
Dependability	Clear articulation of the research design that would allow another to repeat it, in another setting	Methods have been described in detail Questionnaires and focus group interview schedule available for scrutiny
	Operational detail of data gathering discussed	Research report provided detailed account of data gathering and management.
	Reflective appraisal of the project	Discussion is provided relating to study weaknesses and strengths
Confirmability	All steps taken to reduce researcher bias	Investigator preconceptions have been stated in the research report as part of the reflexive considerations. Weaknesses have been reported in method and analysis
Transferability	Information must be given to enable other researchers to assess the applicability of the results to other contexts	The number of organisations taking part is stated The number of participants involved are stated Description of data collection tools and methods made clear The number and length of data collection sessions The time period over which the data was collected

3.30 Analysis of data

The focus group facilitators were instructed first to transcribe the tape recordings verbatim into their own language, to validate these with their groups and then to translate this into English before sending them to myself and the other researchers. Each of us coded the transcripts separately and identified themes emerging from the data individually. We then met to discuss each analysis as the group transcripts were produced. The researchers included myself, Dr Mahmoud and Ms Rivers.

3.31 Coding of transcripts

The process of constant comparison analysis was adopted as the method of formulating the constructs and themes that emerged from the data. I began by using open coding to derive and describe initial concepts in order to begin to build the themes that would answer the research questions. This technique, which has its roots in grounded theory was first used and developed by Glaser and Strauss in the late 1960s. I began by reading each of the transcripts many times, and attached conceptual labels to the phenomena as they emerged(99). During this process, 'data are broken down, scrutinised and compared for similarities and differences(99)'. Questions are then asked about the emerging phenomena, as reflected in the data. This first step was conducted entirely by hand and by using a numbering system. The transcripts were broken down line by line, where possible, and questions were asked about the data where appropriate. For example, I asked, 'what does this mean? What does this tell

me? Or what is this about? Each ‘bit’, was given a number. If subsequent ‘bits’ seemed to correspond to previous ‘bits’ then the same number was allocated to that piece of data. A ‘bit’ constituted a word, a sentence or a section of speech from a respondent. This enabled me to build categories and group together the labelled concepts. Differences and similarities were compared in our analysis during a series of meetings to discuss our findings. The constructed themes were then fed back to the facilitators and they were asked to validate the findings with their respective groups. They did this by explaining in their own language the themes we had identified, and were asked to report that they recognised these as their own stories and that they reflected an accurate synthesis of their discussion.

3.32 Findings

3.32.1 The Community response: Questions 1 and 2

1. How does the community experience influence disease prevalence of TB among refugees, asylum seekers and homeless people in Brent (high risk groups)?
2. How do cultural and social factors in different refugee communities influence willingness to be treated or seek help?

One hundred and four (104) participants took part in ten community focus groups including women only sessions; eleven General Practitioners and five nurses participated in the study. The ethnic mix of those who took part is shown in Figure 5 on page 51.

Five main themes were identified as being fundamental to the way communities perceived and reacted to TB and these were derived from the community stories and in some cases supported by the views of the professional groups. The themes that emerged were broadly reflected as history and memory, stigma, TB as a bio- medical disease, TB as divine punishment and social and cultural factors. Sub- themes were also identified supported these main areas. An overview of the themes and how the subthemes related to them are described in Table 7. Knowledge of Tuberculosis differed within the groups in terms of their understanding of modes of transmission, the nature of the condition, its ‘treatability’ and common risk factors. The impact of knowledge and how it related to the focus group opinion will be reported and

discussed later. First, I would like to explore the themes that emerged from the focus group interviews and the relationship of the sub-themes. Within the explanatory section, words highlighted in italics represent items that formed significant elements of the themes or sub-themes of each category.

Table 7: Main themes and sub themes

History and Memory	Stigma	TB as biomedical disease	Divine punishment	Cultural and social factors
TB and Poverty	Labelling	Transmitted by coughing and sneezing bacterial)	Poor practitioners of faith	Drinking, smoking, drug use including Khat use
TB and AIDS	Being marked for life	Prognosis and treatment	Not praying enough	Poverty and poor living conditions
TB and death	Concealment of disease	Affects the lungs and other parts of the body	Wrong doing	Sharing cups and plates
Confidentiality	Fear of isolation			Language and translation issues
Drs as police	Divine punishment			Role of traditional healers
	TB and HIV and AIDS			Mismatch in expectation of health providers role

3.33 Theme 1: History and Memory

Memories of the experience of TB in people's homelands will undoubtedly affect their attitude towards TB in their new society. Here, a participant shares their memory of TB, and how anxieties relating ***confidentiality*** and ***death*** serve to act as deterrents to seeking help;

(Somali male)

Somali community regard TB as a dangerous illness because some of them recall those of their families who ***died*** *in Somalia…*

About 10-15 years ago in our home country this illness is regarded as a dangerous disease, it cannot be cured easily, treatment to be continued for about one and a half to two years. Isolation and indoor treatment was compulsory and ***confidentiality*** *cannot be maintained. (sic)*

We found that concerns about difficulty in maintaining ***confidentiality*** in the homeland were transferred to current experience in the migrant setting. This perpetuated the fear surrounding TB, and the social consequences of disclosure, to the host community. In close knit communities where privacy is difficult to maintain this may also deter people from not only seeking help from health professionals, but it may make it difficult to complete their treatment without being identified. Believing that ***confidentiality*** can be difficult to maintain, can lead to extreme measures:

(Somali male)

My cousin was not expecting to be diagnosed with TB. It was rather a shock…. Because of my closeness with my cousin, I had to undertake some tests, which came out negative at that time and has remained so up until now. To protect my cousin, I had to accompany her to the TB centre so ***no one will know*** *who was the infected person between the two of us. I did that in order to protect my cousin, not to be ashamed of her sickness and get the needed support. (sic)*

Experiences from the past were not confined to a specific group. A member of the Afghan group recalled the following event from his homeland:

(Afghan male)

An Afghan in Kwiet was ***died*** *of it and the authority were not allowing him to be buried in Kweit and even the authorities in Afghanistan did not allow his family to open his coffin, in the fear of the disease could spread and it would be much safe to bury the person as soon as possible. (sic)*

A Somali man remembers:

(Somali male)

*They didn't speak about it and no one asked him about it. And this neighbour is now**...is passed.** He is **dead** now..and..eh..till now they did not say that he had TB and they wouldn't bring him to the hospital. (sic)*

3.33.1.1 Sub-theme: Health workers as authorities and police and TB and death

The above quote also highlights another important element of past experience that might influence how communities respond to TB. The knowledge that people ***die*** from Tuberculosis, and the poor treatment and stigma afforded to those who are afflicted, does little to foster good relationships with those whom are viewed as ***'authorities'*** in their homeland and the new migrant situation. Unfortunately it was expressed that doctors are often viewed as authorities or the police. People are naturally cautious and mistrusting of ***authorities*** if they are aware of bad treatment or have been badly treated themselves. Many refugees have experienced severe trauma, loss and displacement and may have good reason to fear those who are perceived to be in authority. The GPS discussed this problem in detail and claimed that migrant groups often confuse health workers with regulators and 'police' which adds a complex dynamic to the patient /doctor relationship. The GPs resented being in a position where they were required to assess the refugee status of patients before they could be treated and recognised that the conflict of interest undermined the therapeutic relationship

GP:

*The first thing is to get them in the door as it were...now obviously we are an **authority,** they have to answer some questions, are you a refugee or whatever..we are not allowed to take anyone just like that anymore. (sic)*

Another GP reports:

*We are not **policemen**! We don't want to be **policeman** as doctors...we don't have that role...you said yourself right at the beginning people are frightened of all sorts of stigma and stuff...if we start getting too particular about things ..they will go away*

from us and they won't get the healthcare they need. It jeopardises the thing right from the beginning. No, it should be the home office and the immigration people, they re the point, they are the policeman they should be doing this....we can't be ***policeman****. (sic)*

The combination of past experience from homeland and memories of poor treatment during the migrant journey present a complex set of barriers for health workers and patients alike, against a background of a socially complex condition such as TB. One GP offered a solution:

I think the immigration authorities ought to put a stamp in someone's passport when they come into the country, like a sort of code that says exactly what they are entitled to, and then that would be the end of it.. (sic)

3.33.1.2 Sub- theme: The association of TB with poverty

The idea that poverty was the primary source of Tuberculosis was also associated with homeland experience. A group leader who ran the Kiswahili speaking focus group summarised the response as follows:

Group leader following focus group discussion including members from Uganda, Kenya and the democratic republic of Congo:

Most Africans associate ***TB with poverty****, therefore resign themselves to* ***death*** *once diagnosed with TB, Unfortunately, this mentality has been carried forward by Africans living in the western world especially amongst the Kiswahili speaking community in Brent . Although many argue that there is no TB awareness for them to do anything about it, even if the opportunity is presented they do not take it. The common reason for failing is stigmatisation...the fear of being rejected and isolated by their own community. (sic)*

3.33.1.3 Sub-theme: TB and AIDS

Another important reason reported why there may be a strong negative response to Tuberculosis is related to the perceived relationship between HIV and AIDS and the assumed social behaviours that this dual diagnosis might suggest .The HIV and AIDS group reported the following:

HIV and AIDS Group member:

*Those who were found to be infected with TB will be isolated by the community if someone has caught TB, people will generally assume that they have **HIV/AIDS**. (sic)*

In Africa, where the dual diagnosis of HIV/AIDS and TB is a reality, this association is easy to understand:

African French speaking group member:

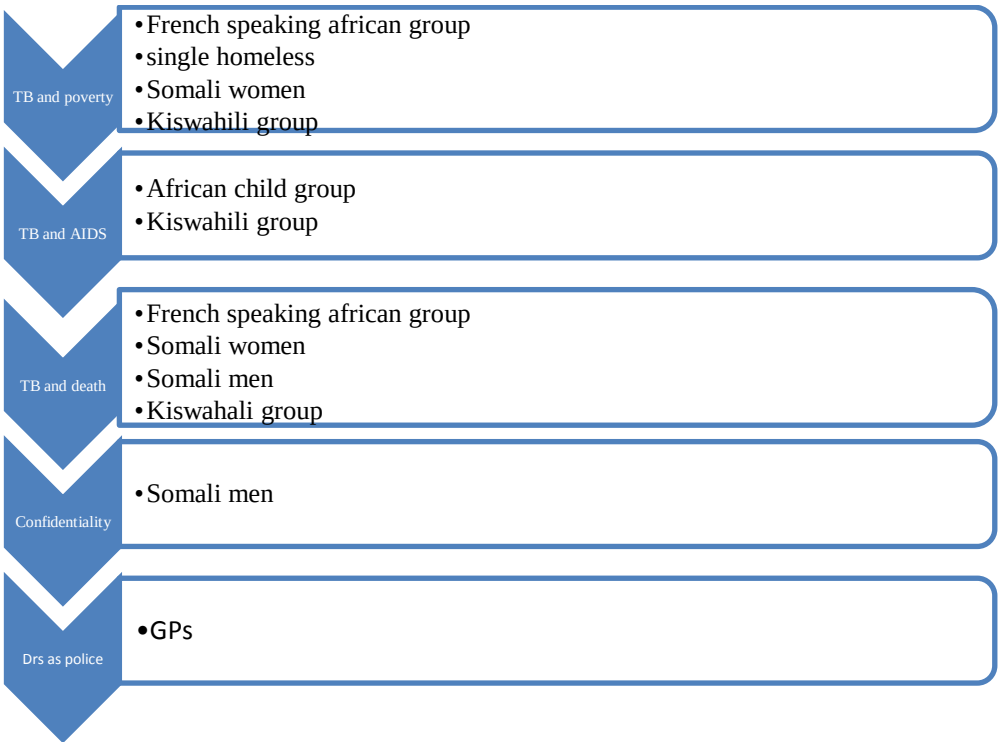
*My half sister was infected with TB and her mother refused to tell anyone in the family. We were told that my sister was sick and needed to travel to one of the cities in the Congo to rest. It was only when she **died** that the truth was revealed..she had **AIDS**. (sic)*

One suggested reason for this secrecy lies in the assumptions held by certain community groups regarding taboo behaviour that might lead to HIV infection:

*No one wants to be identified as having **HIV/AIDS** due to the belief that it is a disease contracted due to promiscuity. Since the community believes that TB is associated with **HIV/AIDS**, it bears a very negative response from the community due to stigmatisation. (sic)*

The factors that make up the theme of history and memory demonstrate that previous experience can determine behaviour and affect willingness to seek help from health workers for a variety of reasons. Many other respondents did report that they would seek help from their GPs or the hospital if they thought that they might have symptoms of Tuberculosis and not all people believed that TB was synonymous with AIDS. It was noted by the research team that those who would not hesitate to seek help from health workers were generally better informed and had more knowledge about Tuberculosis in general and this helped to dispel any myths and fear that surrounded the disease. Figure 7 shows the subthemes described as health beliefs that emerged from the focus group stories. The theme of history and memory and the concerns brought about by previous homeland experience are summarised in Figure 7:

Figure 7: Theme: History and memory



3.33.2 Theme 2: Stigma

Some respondents talked of 'taboo' and 'shame' as much as others related to stigma. We wanted to specifically understand what was stigmatising about Tuberculosis in our target communities. The members of all groups talked about stigma and taboo as powerful social forces that shaped the community response to Tuberculosis.

Within the data, sub themes were identified that highlighted the different aspects of stigma or taboo that were talked about. These included ***labelling***, ***fear of isolation***, ***concealment of disease***, ***punishment from God,*** and being '***marked for life'***.

3.34 Sub-theme: Labelling

The concept of labelling as being part of the stigmatising process was consistent with our findings. One participant reported the local culture of fear that had evolved around the chest clinic where patients were being screened, treated and followed up.

(Somali women's group)

Participant: I don't know what that hospital does or even its name, yes the -------- one, well when I came here I was told that some newly arrived people were sent there and escaped from the nurse, as they did not want to be seen in that clinic…. (Laughter) I guess they did not want to be ***labelled,*** *right, but I was told I should not even look at it when I am passing.. I was so paranoid" (sic)*

The fear of being labelled was so strong in this respondents view with the nurse being identified as someone to 'escape from'. The use of the word ***'escape'*** is interesting too given the view reported earlier that GPs often felt they were perceived as the police. The idea of 'escape' is congruent with the metaphor of imprisonment, with health workers as the police and the patient desiring freedom. It is difficult to know how much this reflects an error of translation or whether it genuinely reflects a harmful community perspective. Undoubtedly the combination of both presents real challenges to successful healthcare engagement. This perspective could easily result in some members of the community failing to seek help if they became ill, as they would fear being perceived as outcasts. It may be that the fear of healthcare professionals expressed here is a reflection of the healthcare professional as an authoritative figure or it could be derived from the knowledge within the community that the clinic was a place where people were treated for Tuberculosis, therefore being seen could lead to stigmatisation.

3.35 Sub-theme: Concealment of disease

Increasingly, as individuals experience stigma, they are less likely to seek help or disclose to others that they are ill. ***Concealment***, even if treatment starts, can become a barrier leading to poor adherence with treatment and increased risk to others.

(Afghan group)*:*

Participant 1: A TB victim always ***avoids to be identified****. He regards himself an* ***outcast*** *because if his community regard TB as a dangerous illness that is why a TB victim* ***is isolated*** *(sic).*

The experience of being isolated in this way can be deeply damaging to individual and community identity, a particularly important consideration in refugee and asylum seeker communities where solidarity and social support are important in helping people cope with everyday life and, ultimately, survival. Adaptation to a new life requires acceptance and support from community peers:

(Somali male group):

Group leader: Is there any fear about TB in your community?

Participant: Yes, because some people think that if they catch TB they will be ***shunned*** *for the rest of their lives (sic). (Somali male)*

3.36 Sub-theme: Being marked for life

The idea that the stigma of TB is long lasting in some communities provides all the more reason to avoid being diagnosed:

(Tamil group):

Participant 1: Even after the disease is treated and cured fully, the person is ***nicknamed*** *as '****TB man'*** *for the rest of his life. People are reluctant to accept money, notes and coins from them, even after the disease is treated and cured fully' (sic)..*

3.37 Sub-theme: Fear of isolation

The isolation experienced and remembered by some participants supports the idea of long lasting stigma that prevents reintegration with society and acceptance by the patients host community:

(Tamil Group leader): *Another member said that he knew a person who took treatment at a sanatorium and now he is leading a normal life, yet he still remains* ***isolated*** *from other people. (sic)*

And a Somali woman relates:

Participant: People treat patients (people with TB) very differently and ***don't come anywhere near them*** *really-people think that person is suffering from a VERY bad*

condition and will not see that person in the same way anymore (sic).(Somali women's group)

This view was evident across the different groups. In the French speaking African group a respondent reports:

African French speaking respondent:

*Tuberculosis is a taboo subject. People are **afraid to approach** sick persons and even to talk to them….There is **fear** and **shame**. People are afraid of catching the sickness and the sick person is **not welcomed**, he is **rejected.** (sic)*

As discussed earlier, one reason that may partially explain this taboo and stigma associated with Tuberculosis is the association with HIV and AIDS:

(African child group):

*Participant: Nowadays, people tend to think that if someone catches TB definitely the person is contaminated with **HIV/AIDS** as well. My half sister was infected with TB and her mother refused to tell anyone about it. We were told that my sister is sick and needed to travel to one of the cities in the Congo to rest. It was only when she dies that the truth was revealed. She died from AIDS (sic).*

In Muslim communities, the presence of HIV/AIDS can indicate sex before marriage and infidelity within marriage; both of which are totally prohibited. The association of Tuberculosis with HIV/AIDS therefore will have special resonance with these groups. Some group members were aware though that the presence of Tuberculosis did not necessarily mean that HIV was also present:

(Kiswahili group):

Participant: The community needs to know that one can be infected with TB without HIV and AIDS, although HIV and AIDS sufferers may become infected with TB (sic)

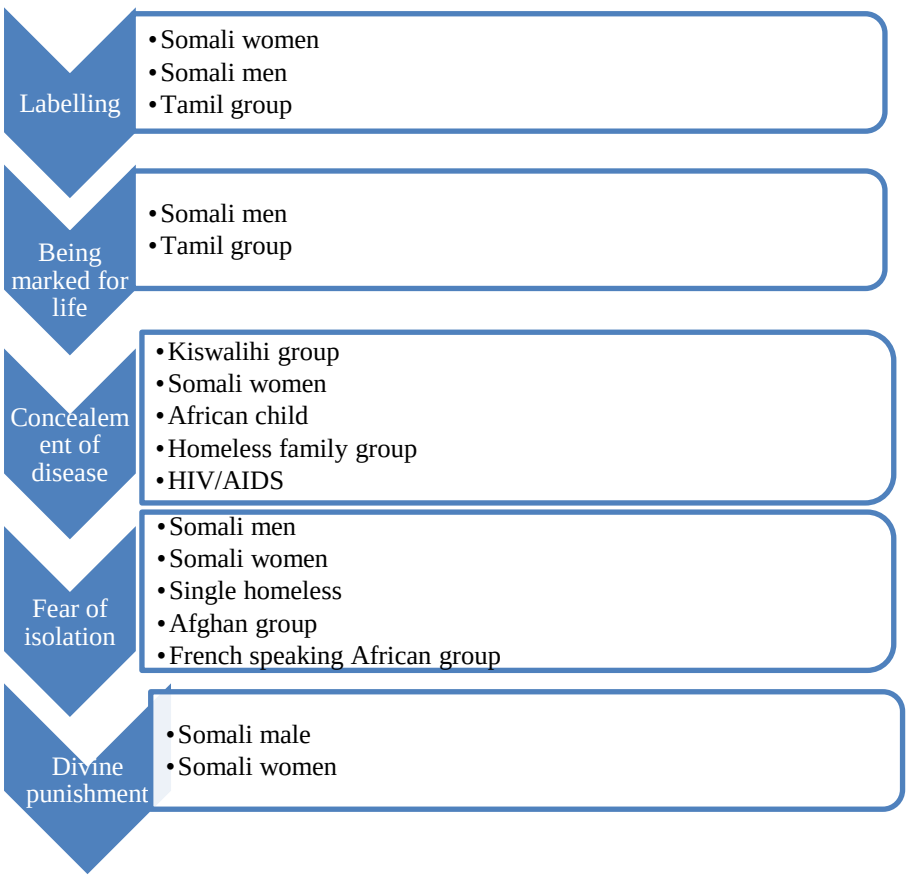
3.38 Sub theme: Divine punishment

The idea that Tuberculosis was punishment from God for wrong doing is later explored as a theme by itself to reflect its importance in potentially influencing

responses to Tuberculosis. TB as divine punishment however, also constitutes an important component to the stigma surrounding Tuberculosis, particularly in devout communities where ideas of goodness and godliness are based upon strict adherence to religious codes of practice. I shall explore this idea more in addressing the idea of Tuberculosis as divine punishment later on in this chapter.

Many ways of understanding Tuberculosis, its causes and associations seem important to the construction of stigma in relation to the disease. The association of Tuberculosis with HIV and the taboo experienced in African communities in particular, because of this association is reflected elsewhere in the literature (100). Tuberculosis as punishment from God is also an important contributor to the stigma of Tuberculosis in communities where religious integrity is central to the way of life, such as the Somali community. Figure 8 shows how these elements of stigma were reflected in the various community groups:

Figure 8: Perception of stigma and sub themes of stigma as expressed by community groups



3.39 Theme 3: Tuberculosis as a biomedical disease

The concept of Tuberculosis as a bio-medical condition strongly emerged in the focus group discussions. Most groups understood Tuberculosis as a contagious disease, transmitted by coughing and sneezing that in most cases could be treated with antibiotics. When asked, in the focus group discussions 'what causes Tuberculosis?' many people knew that it was a disease that can *'affect the lungs'* as well as *'other parts of the body'*. Words and ideas expressed by the groups congruent with an understanding of Tuberculosis as a medical condition are highlighted in the text in bold and in italics. The single homeless group recognised that it was a highly contagious but curable condition.

Single homeless group:

Participant 1*: People spread the condition by* ***coughing*** *on the buses and* ***sneezing*** *(sic)* and

Participant 2: *TB is a* ***disease****. You can take the medicine and then you will be fine(sic).*

All groups reported in their focus group interviews that Tuberculosis could be successfully treated with antibiotics although within groups there were also members who described TB as incurable. This is not incorrect *per se*, as there are some strains of the TB that have become resistant to available treatment (MDR TB). It was difficult to ascertain from the transcripts whether this was known or whether there was a genuine belief that all TB was incurable. Many of the groups knew that common symptoms of Tuberculosis included weight loss, night sweats and coughing. The Somali male group reported that Tuberculosis could be treated by using '*herbal remedies and Koran healing'*. The same group however reported that *'conventional medicine was the best treatment for TB',* supporting an understanding of Tuberculosis as a biological disease process. The single homeless group displayed a good level of understanding around Tuberculosis, its causes and treatment:

Single homeless group:

First of all Tuberculosis is a common ***disease*** *especially in hot countries. It is common in Africa and is a* ***transferable disease*** *(sic).*

The use of the word ‘epidemic’ in another respondent’s view showed relatively sophisticated understanding of the biomedical view:

*This is an **epidemic sickness** that can **spread** from one person to another (sic).*

Knowledge of symptoms was also reported. The use of the word ‘slim’ reveals awareness around weight loss as an important symptom of TB:

*This is a serious **sickness.** The people who have it are **coughing** too much and they are **slim** (sic).*

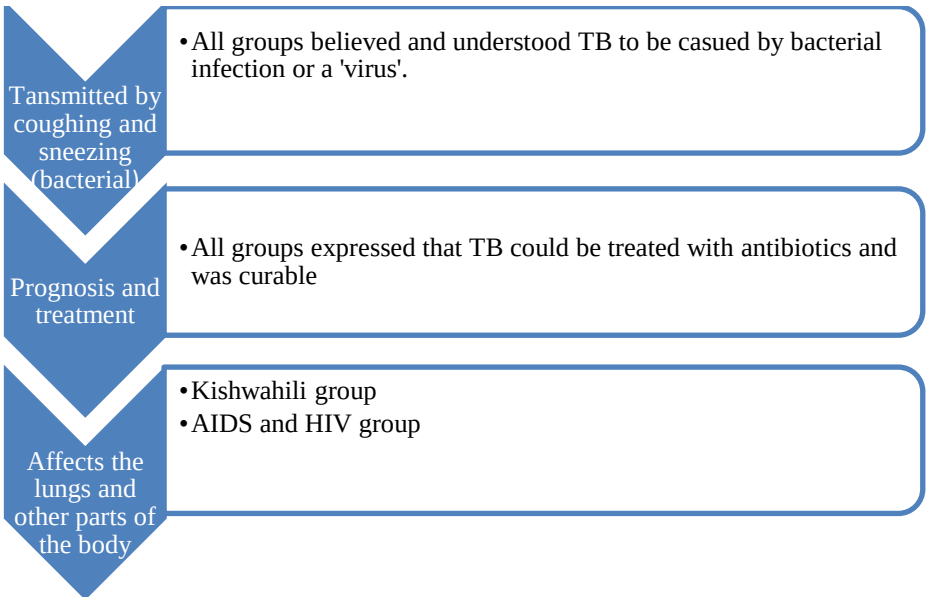
And:

*TB is just a **bacteria** which grows in your body. Once you get it, you can **spread** it to people. You can get it from smoking (sic).*

There were no reports of Tuberculosis resulting from witchcraft or sorcery as described elsewhere in the literature. It maybe however that these ideas are very particular to specific groups of people not represented in my sample.

A summary of the findings and construction of this theme are presented in Figure 9:

Figure 9: Tuberculosis as bio-medical disease



3.40 Theme 4: Divine Punishment

The belief that Tuberculosis was punishment from God for wrong doing was a strong theme in the stories and was especially resonant among the Muslim groups and particularly evident in the Somali group who associated Tuberculosis with being a poor practitioner of faith. As previously highlighted this belief did not exclude understanding of Tuberculosis as a disease caused by bacterium. Participants who held this view that Tuberculosis was caused by God also reported that prayer and Koran healing were effective strategies in the treatment of Tuberculosis. I hypothesize that this may add further to the complexity of the stigma of Tuberculosis for individuals who not only suffer being isolated and shunned from their communities but are also labelled as 'un-virtuous' or sinful:

(Somali male group):

Participant 1: I believe TB is caused by different reasons including lack of hygiene, lack of enough food and lack of prayers.(sic)

Participant 2: Yes I agree, but TB is also a curse from Allah when people ignore his way of life or don't worship him then TB spreads.(sic)

Participant 3: Yes, TB is a kind of punishment form Allah and people give advice to be pious and maintain links with Allah.(sic)

Participant 4: TB could be healed by using herbal medicines and Quran healing. (sic)

Participants reported that the fear of isolation and public 'shunning' associated with Tuberculosis may encourage consultation with spiritual or faith healers rather than seeking the help of conventional doctors. This could potentially occur in the migrant setting, although I heard no reports of this in London, but participants did report that this was common practice in their homelands. Some participants reported that they had confidence in such practices and that people often consulted with elders in the community first before seeking help from a doctor. The association of sickness with 'divine punishment' is likely to reinforce this behaviour among communities who believe it is not necessarily a doctor's jurisdiction to treat Tuberculosis.

(Somali male group):

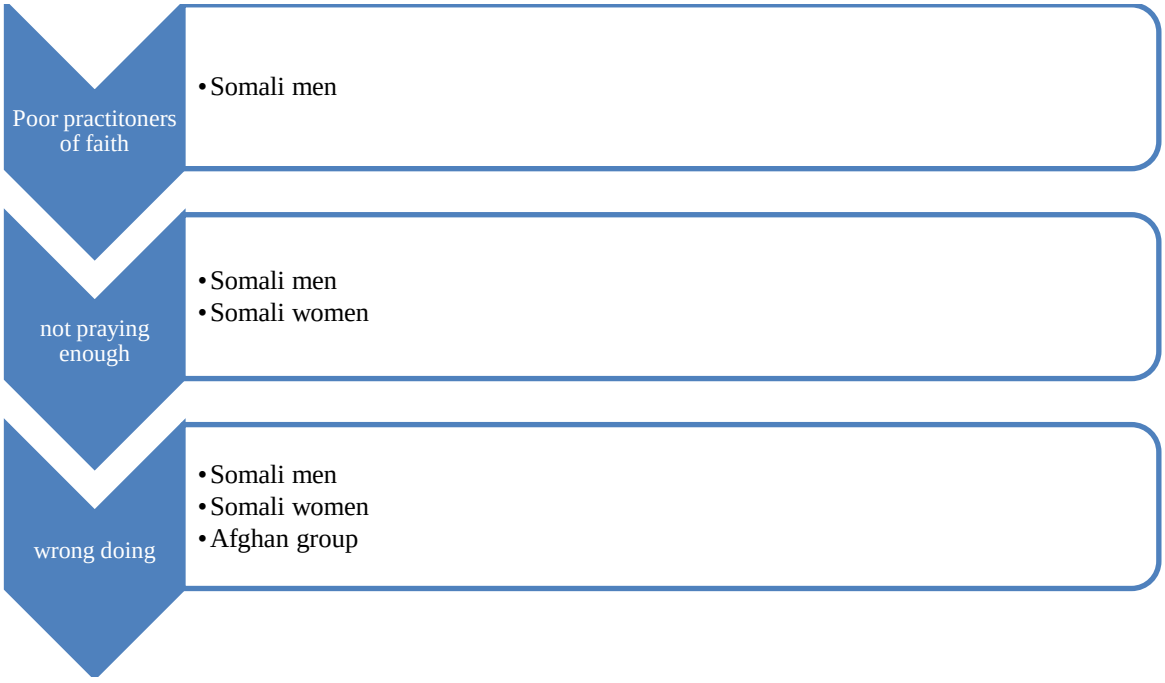
Participant 1: People will consult a traditional healer because they will go unnoticed. No one will discover their secret. We have never heard of anyone being cured by traditional medicine but we know that healers can ease the pain.(sic)

Participant 2: In Somalia, especially the nomadic people use their own medication for treating a TB victim. The patient is put in a separate place where he stays alone for a period of minimum 3-6 months. He is fed with fresh goat, sheep and camel meat. He drinks camel milk for the whole period. The Somali regard the camel milk as a special cure for TB.(sic)

Figure 10 identifies the components of divine punishment that were talked about and the groups that most identified with this idea.

Figure 10: Divine punishment

Health belief **Community group**



3.41 Theme 5: Cultural and social factors influencing willingness to be treated.

In response to research question 2, we asked the community groups 'how does your community respond to TB socially, is it seen as a negative thing?' And we asked the professional groups whether there were any cultural issues that affected their ability to effectively treat patients and more general questions around the causes of delays to diagnosis, treatment and follow-up (appendix 5). Both the community and the professional groups provided enlightening responses to these questions. There were many social factors discussed and few cultural examples provided. The cultural elements are discussed later on in this thesis, as they may not, in themselves provide any barrier to successful treatment. It does seem however, that there were significant social factors that, both community and professional groups cited as significant barriers to successful treatment.

Social conditions featured highly as being perceived as significant in the transmission of disease. Poverty, lack of cleanliness *'bad drains and nasty living conditions'* were cited by the single homeless group as significant factors. One member from this group also felt that the only reason that a cure for TB had been found, was a result of the resurgence of the disease in wealthy western countries suggesting too, a perceived political element, which unfortunately was based upon a misconception that a cure was a recent advancement in modern medicine:

(Single homeless group):

TB only affects people living in poor countries. It's only because it's on the rise in the UK and the USA that a cure has been found. It's taken too long to find a cure'! (Sic)

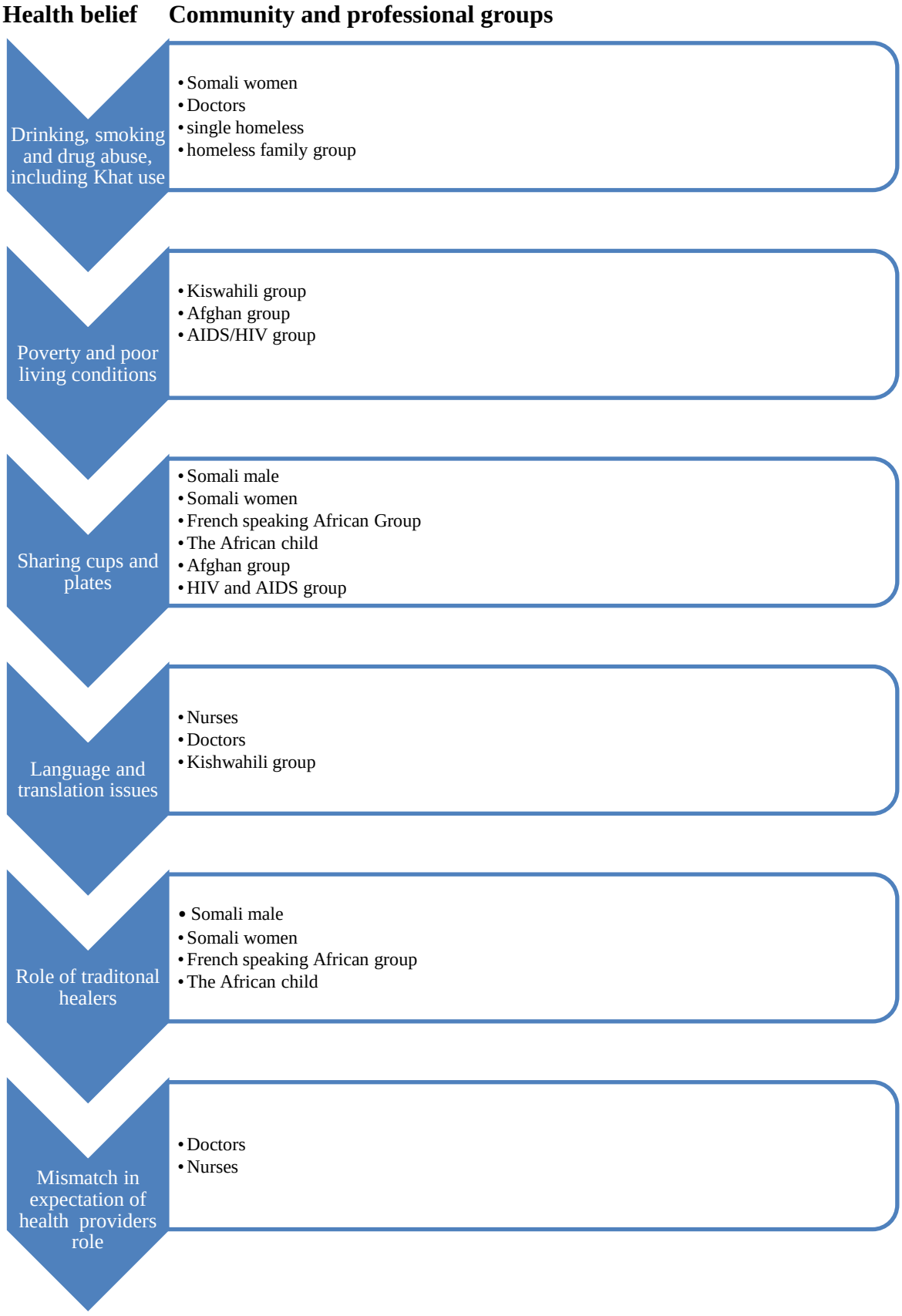
The single homeless group also recognised and discussed the significance of 'rough sleeping' as an important factor in 'weakening immunity'. It was also reported that many homeless people may have other social and personal difficulties that will take precedence over seeking help for any illness.

(Single homeless group):

'Some homeless don't care about TB. Only care about where they are going to get the next drink from or some other kind of drug' (sic).

The perception that poverty was important in the aetiology of Tuberculosis was discussed by many of the groups and although forms part of the sub theme for history and memory, poverty was also talked about as an important factor in contemporary life. The Afghan reported that they considered *'damp and crowded conditions'* ideal for the transmission of disease. Damp and crowded conditions were also mentioned by the AIDS/HIV group as well as *'extreme cold and dampness'.* Members from the Kiswahili speaking group reported that language problems were, in general significant factors influencing communication between care providers and members of the community. Figure 11 identifies the elements of social and cultural life identified by the groups that may impact and influence disease prevalence and influence people's ability to seek help. These elements will now be discussed further.

Figure 11: Social and cultural factors



3.42 Summary of themes

One can begin to see how the various themes overlapped. For example, some elements of stigma resonated with the theme of history and memory, as some perceptions associated with stigma resulted from the fear of isolation and social shunning experienced back in homeland countries. The theme of divine punishment influenced the possibility of stigma through the idea that those with Tuberculosis from certain communities were being punished for wrong doing or were poor practitioners of their faith and therefore un- virtuous. The association of HIV/AIDS overlapped with the memories that some held of who was affected by Tuberculosis back in their homelands and this too impacted on the stigma surrounding the condition. Despite some of these misconceptions or in some cases, justified fears (the association of TB and AIDS for example), most people understood Tuberculosis as a bio-medical condition, even those who expressed a strong affiliation with the idea of TB as divine punishment. Social and cultural factors were cited by all groups who took part in the focus group discussions as being important to both the risk of Tuberculosis and the successful treatment of the condition and included some misconceptions about transmission; i.e. sharing cups and plates and a legitimate role for traditional healers in the treatment of Tuberculosis. Social and cultural factors cited by the health professionals that affected the potential for successful treatment related to problems surrounding language and translation as well as a mismatch in the expectation of some patients and the reality of the health and social care, health providers were able to deliver. I will now go on to discuss the element of knowledge in this study, how it was measured and how the emergent data was used to triangulate the findings of this research.

3.43 Knowledge of Tuberculosis

The assessment of knowledge emerged from the data in two ways. First of the all, the questionnaire contained a thirteen item set of statements corresponding to common areas of misconception as well as important aspects of Tuberculosis knowledge such as facts about contagion and transmission and how the condition is treated. The statements were expressed as closed statements that the participants were asked to rate ‘true or false’. The statements were derived both from the literature and from clinical guidelines and reflected common misconceptions about the disease as well as clinical

facts. Given that poor knowledge about Tuberculosis is an important factor in driving appropriate health seeking behaviour and therefore represents a 'barrier' to appropriate case identification and treatment, this was an important area to investigate as part of the overall assessment of barriers(29;45;59;101). Knowledge measurement was included to support findings for research question number 3 in particular which asked: *What are the barriers that may affect the uptake and service delivery to asylum seekers, refugees and homeless people?*

3.44 Validity and reliability of knowledge measurement

Research instruments employed in the measurement of any concept should be tested for their reliability and validity to ensure that they measure what they intend to measure and that they consistently measure the concepts under study(102;103). Test for *'content'* validity, i.e., that the domain of the subject area has been adequately covered and *'construct*' validity, the extent to which the measurement conforms to existing ideas about the concept being measured(103) are identified as important elements in the design of any instrument. In addressing the *content* validity of the 10 item section, knowledge of TB was operationalised as having components related to factual statements that corresponded to its biological identity and prognosis; i.e. TB as 'an infectious treatable bacterial infection' as well as routes of transmission, common risk factors and the realities of treatment. Usually, the constructs identified to represent the concept of knowledge for example, would require thorough testing within the target populations. Unfortunately, I was unable to systematically validate the items due to the limited recourses. Each item was therefore considered 'valid' if the source of each statement corresponded to clinical guidance (what is known in science, i.e., a 'statement of fact') and reports in the literature relating to perceived misconceptions. Some of the papers included in the construction of this item were from different settings other than London and reflected the views of people in other parts of the world. Although it is true that these beliefs and misconceptions may not have been transferable to my intended population, this also provides a good reason to include them; to see how relevant they are in the target community. Given the diversity of the Brent population, knowledge constructs derived from other global settings expressed by communities experiencing Tuberculosis seemed appropriate.

Table 8 shows how the construct validity of the 10 item knowledge elements were assured, and the origins of each as the items as arising from 'misconception' or 'statements of fact'.

Table 8: Construct validity of knowledge items

Item	Rationale for inclusion	Item type	Source
Biological construct: 'TB is infectious' **true**	The knowledge that TB is infectious is important as it could support early health seeking behaviour in those with symptoms and the appropriate management of contacts	Statement of fact	Literature (104)
Transmission construct :'TB can be transmitted by shaking hands' **false**	The misconception can lead to inappropriate avoidance behaviour of infected individuals and re-enforce stigma	Misconception	Literature (105)
Biological construct: TB 'Can be transmitted by coughing and sneezing' **true**	Routes and mode of transmission are important in influencing appropriate health seeking behaviour	Statement of fact	Clinical guidelines (104)
Transmission construct: 'TB Can be transmitted by eating together' **false**	Close and prolonged contact with infected parties may increase exposure time which could be significant in increasing the risk of transmission. Eating together in itself is not a risk	Misconception	Literature (101;105;106)
Biological construct: 'TB can affect any part of the body' **true**	Awareness that TB can manifest in parts of the body other than the lungs may lead to increased case identification in the recognition of such symptoms, such as swollen glands	Statement of fact	Clinical guidelines (104)
Transmission construct :'TB is punishment from God' **false**	This belief may lead to unhelpful stigma and isolation of those affected and may influence what sort of health provider people seek out. I.e., preference for traditional healers	Misconception	Literature (44)

Item	Rationale for inclusion	Item type	Source
Biological construct :'TB is incurable' **false**	Belief that TB is not curable may lead to unhelpful avoidance of infected individuals and create fear within those affected	Statement of fact (TB is mostly curable)	Literature and clinical guidelines (29;104)
Treatment construct :'TB can be treated by traditional healers' **false**	This belief may influence choice of health provider and delay medical diagnosis and effective treatment	Misconception	Literature (44;106)
Risk factor construct: 'HIV infection increases the risk of TB' **true**	Helps identify those most at risk	Statement of fact	Clinical guidelines (29;104)
Transmission construct 'TB runs in families' **false**	The belief that TB is hereditary may lead to unhelpful avoidance behaviour of those infected/affected and have possible social/cultural consequences	Misconception	Literature (44;105)
Risk factor construct: 'Risk of TB increases in cold weather' **false**	Misconceptions around transmission and causes of TB can influence behaviour and deflect people's attention from the genuine risks	Misconception	Literature (47)
Risk factor construct: 'smoking increases the risk of TB' **true**	Knowledge regarding genuine risk factors can lead to people choosing positive health behaviours such as quitting smoking	Statement of fact	Literature and clinical guidelines (12;106)
Risk factor construct: 'TB affects only the poor' ***false***	Misconceptions about who is at risk could lead to complacence and possible missed diagnosis. TB can affect anyone	Statement of fact	Clinical guidelines(29)

In terms of the reliability of the instrument this was more difficult to assure, given the added complexity that the concepts being measured may not have been directly transferable to other languages and therefore may have become ambiguous or misleading. This may have undermined the consistency and test-retest reliability (stability) of the knowledge instrument and I acknowledge this as a weakness. The

resources that were required to test the reliability and validity of the questionnaire in the various languages spoken by the participants were outside the available resources of this work.

3.45 Results from knowledge questionnaire

Knowledge of Tuberculosis signs, symptoms and treatment varied among groups and within groups. As well as the focus group themes I wanted to explore how the opinions expressed by the groups related to their basic knowledge of Tuberculosis as measured by a more objective tool. Accurate knowledge of these elements can reduce fear, misconception and possible stigma associated with the condition. For instance, one respondent cited earlier in the example illustrating the relationship between HIV and Tuberculosis reported that people needed to understand that the two conditions were not necessarily linked. This knowledge enabled the respondent to make a separation between the two conditions and therefore potentially avoid the stigma that arose from that misconception. It must be noted however, that this belief is not entirely unreasonable as in Africa especially; there is a pronounced co-morbidity of HIV and Tuberculosis.

Using the thirteen- point true or false item, I was able to triangulate the knowledge findings of the community groups with the focus group discussions. Table 9 to Table 18 summarise the responses to the knowledge questions. These are presented individually to illustrate some of the differences that were evident between groups. This triangulation allowed some interesting contradictions to emerge. For instance, whilst the Somali men and women were most likely to conceptualise Tuberculosis as a disease ‘caused by God’, a belief which could be reasonably identified as equating to poor knowledge or misconception; all of the Somali men and women understood that Tuberculosis was an infectious disease, transmitted by coughing and sneezing (table 6 and 12). In the focus group sessions, the Somali men spoke about Tuberculosis as punishment from God and the belief that the disease was sent by God as a punishment for wrong doing. It is interesting to note, that the idea of Tuberculosis as a bio-medical condition, does not exclude belief relating to divine punishment. This finding supports the work of other researchers that have explored the issue of Tuberculosis stigma in the Somali community(44). 50% of the Somali men thought

that Tuberculosis was incurable and 60% in the Somali male group believed that Tuberculosis could be transmitted by shaking hands.

In the other groups important misconceptions included the belief that Tuberculosis could be treated by traditional healers (40% of the HIV group, Table 13; 50% Somali male group, Table 12; and 40% Tamil group, Table 9). Although at first the understanding and belief that Tuberculosis could be treated in this way may be no different than the view that alternative medicine can be used to treat illness in the west, the danger arises from the potential consequence of this belief, in that it may delay consultation with qualified medical staff and therefore delay diagnosis.

3.46 Summary of knowledge of TB among Focus group participants

Table 9: Tamil group (10)

Statement	true	false	Do not know
TB is infectious	10	0	0
Can be transmitted by shaking hands	1	9	0
Can be transmitted by sneezing & coughing	10	0	0
Can be transmitted by eating together	4	6	0
TB can affect any part of your body	9	1	0
TB is punishment from God	0	10	0
TB is incurable	2	8	0
Can be treated by traditional medicine	4	6	0
HIV infection increases the risk of TB	9	1	0
TB runs in families	3	7	0
Risk of TB increases in cold weather	2	6	2
Smoking increases the risk of TB	8	0	2
TB affects only the poor	0	10	0

Table 10: Homeless family group (15)

Statement	true	false	Do not know
TB is infectious	10	1	4
Can be transmitted by shaking hands	1	8	6
Can be transmitted by sneezing & coughing	11	0	4
Can be transmitted by eating together	3	5	7
TB can affect any part of your body	4	2	9
TB is punishment from God	0	11	4
TB is incurable	0	10	5
Can be treated by traditional medicine	2	1	12
HIV infection increases the risk of TB	1	2	12
TB runs in families	2	4	9
Risk of TB increases in cold weather	3	1	11
Smoking increases the risk of TB	3	1	11
TB affects only the poor	1	11	3

Table 11: African Kiswalihi speaking group (9)

Statement	True	False	Don’t know
TB is infectious	9	0	0
Can be transmitted by shaking hands	0	6	4
Can be transmitted by sneezing and coughing	9	0	0
Can be transmitted by eating together	2	5	2
TB can affect any part of your body	9	0	0
TB is punishment from God	0	9	0
TB is incurable	1	6	2
TB can be treated by traditional healers	5	0	4
HIV infection increases the risk of TB	9	0	0
TB runs in families	0	6	3
Risk of TB increases in cold weather	7	2	0
Smoking increases the risk of TB	5	3	1
TB affects only the poor	3	6	0

Table 12: Somali male group (10)

Understanding TB	True	False	Don't know
TB is infectious	10	0	0
Can be transmitted by shaking hands	6	3	1
Can be transmitted by sneezing and coughing	10	0	0
Can be transmitted by eating together	9	0	1
TB can affect any part of the body	7	0	3
TB is punishment from God	4	0	6
TB is Incurable	4	5	1
TB can be treated by traditional healers	5	2	3
HIV infection increases the risk of TB	7	3	0
TB runs in families	7	3	0
Risk of TB increases in cold weather	6	3	1
Smoking increases the risk of TB	6	1	3
TB affects only the poor	6	1	3

Table 13: HIV and AIDS group (10)

Statement	True	False	Do not know
TB is infectious	10	0	0
Can be transmitted by shaking hands	9	1	0
Can be transmitted by sneezing and coughing	10	0	0
Can be transmitted by eating together	5	4	1
TB can affect any part of the body	4	5	1
TB is punishment from God	1	8	1
TB is Incurable	0	9	1
TB can be treated by traditional healers	4	2	4
HIV infection increases the risk of TB	10	0	0
TB runs in families	2	3	4
Risk of TB increases in cold weather	6	0	4
Smoking increases the risk of TB	6	0	4
TB affects only the poor	1	8	1

Table 14: Single Homeless (10)

Statement	True	False	Don't know
TB is infectious	9	1	0
Can be transmitted by shaking hands	2	8	0
Can be transmitted by sneezing and coughing	10	0	0
Can be transmitted by eating together	3	7	0
TB can affect any part of the body	5	5	0
TB is punishment from God	1	8	1
TB is Incurable	3	6	1
TB can be treated by traditional healers	2	5	3
HIV infection increases the risk of TB	8	1	1
TB runs in families	4	4	2
Risk of TB increases in cold weather	4	2	4
Smoking increases the risk of TB	7	0	3
TB affects only the poor	3	7	0

Table 15: Afghan group (10)

Statement	True	False	Don't know
TB is infectious	9	0	1
Can be transmitted by shaking hands	4	3	3
Can be transmitted by sneezing and coughing	7	2	1
Can be transmitted by eating together	4	4	2
TB can affect any part of the body	5	2	3
TB is punishment from God	2	5	3
TB is Incurable	2	6	6
TB can be treated by traditional healers	2	4	4
HIV infection increases the risk of TB	6	0	4
TB runs in families	2	5	5
Risk of TB increases in cold weather	4	2	2
Smoking increases the risk of TB	7	0	2
TB affects only the poor	5	2	2
Comments	Less eating increases chances of TB		

Table 16: French speaking African Group (Angola; Gabon; Ivory Coast; DR of Congo) (11)

Statement	true	false	Do not know
TB is infectious	11	0	0
Can be transmitted by shaking hands	2	6	3
Can be transmitted by sneezing and coughing	8	0	3
Can be transmitted by eating together	9	1	1
TB can affect any part of the body	7	4	0
TB is punishment from God	0	11	0
TB is Incurable	0	11	0
TB can be treated by traditional healers	3	3	5
HIV infection increases the risk of TB	11	0	0
TB runs in families	0	10	1
Risk of TB increases in cold weather	2	6	3
Smoking increases the risk of TB	11	0	0
TB affects only the poor	2	8	1

Table 17: Young People: The African Child group (10)

Statement	True	False	Don’t know
TB is infectious	9	0	1
Can be transmitted by shaking hands	0	8	2
Can be transmitted by sneezing and coughing	8	1	1
Can be transmitted by eating together	5	4	1
TB can affect any part of the body	5	2	3
TB is punishment from God	0	8	2
TB is Incurable	2	6	2
TB can be treated by traditional healers	3	3	4
HIV infection increases the risk of TB	5	2	3
TB runs in families	1	2	7
Risk of TB increases in cold weather	3	0	7
Smoking increases the risk of TB	3	1	6
TB affects only the poor	1	6	2

Table 18: Somali Women's group (9)

Statement	true	false	Do not know
TB is infectious	9	0	0
Can be transmitted by shaking hands	1	6	2
Can be transmitted by sneezing and coughing	8	0	1
Can be transmitted by eating together	4	3	2
TB can affect any part of the body	3	2	4
TB is punishment from God	6	1	2
TB is Incurable	1	6	2
TB can be treated by traditional healers	2	5	2
HIV infection increases the risk of TB	4	3	2
TB runs in families	0	8	1
Risk of TB increases in cold weather	5	2	2
Smoking increases the risk of TB	5	0	4
TB affects only the poor	2	4	3

3.47 Professional experience

The experience of doctors and nurses who are tasked with case identification and providing and ensuring successful completion of treatment represents the other side of the story in terms of teasing out the difficulties and challenges that exist in Brent in managing the Tuberculosis problem. Aside from the community view, the health sector's experience is vital to consider in terms of the provision of care and in explaining some of the barriers that exist to successful case finding and treatment completion. The inclusion of these groups provided data in response to research questions 3 and 4: *what are the barriers that may affect uptake and service delivery to asylum seekers, refugees and homeless people?* And *what are the institutional gaps in prevention, detection, notification, diagnosis, treatment and follow-up?* The interview schedules for the professional groups can be viewed in Appendix 5.

Recurring themes emergent in the professional group included problems with language and translation, access to services, cultural peculiarities and stigma as most likely to affect the identification and management of Tuberculosis. The community groups also reported stigma as important but few commented on any cultural factors that they felt would influence the situation, other than Khat chewing. Expectations about care and what health workers could realistically provide were also discussed in

some detail and this theme was particular to the health professional view. Some aspects of barriers to treatment were discussed only in the professional groups and related specifically to the problems of health care provision in the Brent community.

3.48 Difficulties facing refugees, asylum seekers and health professionals treating Tuberculosis

(Brent GP):

Participant: OK, pulmonary TB is relatively straight forward. You know if you've got glands in someone, you can aspirate or whatever. I'm not sure about the pathways in the hospital though..about being able to pick things up as quickly as you would like..we don't think they actually latch on these things quick enough..I'm not trying to be naughty about this but they don't always pick these things up (sic)

3.49 Financial barriers

On a practical level GPs reported that the financial status of refugees and asylum seekers makes it difficult for patients to cope with repeated visits to GPs, hospitals and the chest clinic. This was seen as a barrier to accessing the necessary services and care required by TB patients and disadvantaged groups in general. GPs felt it was unreasonable to ask financially disadvantaged patients to make journeys to centres that would result in them paying for travel.

(Brent GP):

Participant: I think there's a problem for refugee patients who are hard up, to actually trek from one hospital to another, and some of the services are dispersed. (sic)

3.50 Referral systems

Challenges impacting on the effectiveness of the referral systems were also reported. Referrals to specialists are often quite slow, which may result in some patients being lost, because refugee communities tend to be transient, and by the time their appointment arrives they may have moved on. As a result they may lose their chance

to be seen by specialist medical services. This is further confounded by the delay experienced in obtaining patients records when they change GPs.

(Brent GP):

Participant: You get this hiatus every time you try to get access to the record and it can drag on and on and on… the records then go up and across and there is a delay…

In London a city wide TB register has been established that records all TB cases making it easier for health professionals to track cases.(sic)

This was viewed as very helpful although GPs themselves do not have access to the database:

(Brent GP):

Participant: There is now in place, what we call the London TB Register. If they've lost a patient at least within the London area they will be able to track them (sic)

3.51 Language and translation

Both the GPs and the nurses spoke at length regarding the problems with language and translation as barriers to successful treatment. Difficulties with language often resulted in the use of phone translation systems. It was noted that these systems were unreliable and time consuming. Face to face consultations were preferred but were not always possible. In the absence of a medical translator, family members often stand in to act as translators but this too has its problems:

Participant: … and language is a huge problem, especially with people from all over the place. You have family members who act as interpreters… it's alright, but it's not ideal. In the case of TB there's another issue. People coming from different backgrounds, you tell something to an interpreter and sometimes it takes five minutes to explain it…and you wonder, what are they talking about!? (Laughter by all and agreement) so sometimes, an interpreter for example will be someone who doesn't shorten the story… he might be even giving recommendations to the Patient. (sic)

The nurses made similar observations:

Researcher: *What sort of things do you think are problematic?*

Nurse: *I think the first one probably is language, obviously a lot of people, English is their second language or they can't speak it at all, and sometimes it's very difficult to get interpreters so sometimes you have people turning up to clinics and you have no interpreters, so, its very difficult and really you can't do anything, you have to send them away and bring them back again and that means that you could lose them because obviously, they've come to you and you're turning them away and there's not an incentive to come back. So, there's that problem, there's also using interpreters as well. Sometimes it might be difficult knowing exactly what is being said (sic)*

Both the doctors and the nurses discussed multiple problems with translators and translating systems such as language line.

(Brent GP group):

Focus group leader: *has anyone had any good experiences of using telephones?*

GP: I've used it but it's not very easy

You've got language line. You go back and forward through a third party.

Focus group leader: *How do people find that?*

GP: You have to tell...why you're asking the question and what sort of answer you're expecting otherwise they go on for an hour. You have to brief them about what sort of answer you expect so you know what to ask in the next question. And the interpreter is also interpreting on behalf of the other person. You don't know what's going on!' (Laughter from all)(sic).

The GPs and nurses were concerned about the quality of the interpreters they used and did not have confidence that they related what they wanted to the patient. Some GPs expressed concern that interpreters tended to *'shorten the story'* or '*give their own recommendations*.' The need to provide accurate information to patients regarding diagnosis and treatment is thus undermined by variable language support services.

3.52 Access to health services and expectations of healthcare

From the refugee perspective, access to health services in general and GP services is seen as particularly difficult. The experience of healthcare in other countries is likely to differ in terms of how services are structured and accessed and the role of health care professionals in society. The expectations of doctors are likely to be affected by previous experience. In many countries for example, particularly in African countries, the doctor may be viewed as part of the extended family rather than a state provided service and this can result in very high expectations of health care in a new country. Both doctors and nurses expressed that they felt unable to respond to all the needs presented, especially as some communities expected a full health check. Whilst this expectation may reflect what health providers are able to offer in other countries, health services in the UK are not organised to offer this service. It was universally recognised by GPs and nurses that TB is a complex 'social' disease affecting all areas of a person's life and the parts can be difficult to separate from the whole. These usually include social, emotional and financial variables that will compete for priority in complicated life circumstances. For patients, this amalgam of factors is all part of the same experience, yet health and social services are fragmented, making a cohesive service for patients difficult to access and equally difficult to provide. TB is a disease which is usually associated with poverty, and it is often exacerbated by the underlying deprivation and hardship, that requires a holistic approach if patients are to be successfully treated. Professionals accept the complexity of the clinical and social need of people with TB and services should reflect this picture too.

Participant (nurse): Housing is huge issue… I am not sure how it could be solved……housing, income and applications…the whole system is just fragmented….all over the country; and is not accessible… the family tax credit, the children benefit, the national insurance all are in different places. It took us 7 hours to fill forms. The patient was unable to fill the form. ….she brought us copies of all the paper. (sic)

Participant (nurse): You know, sometimes you feel like they're going away disappointed or… let down, is probably too strong a word but we haven't met their ***expectations i****f you like, because in the end we can't deal with everything. (sic)*

One participant said:

Sometimes it's kind of misinformation somebody comes into the country and is told by someone from their community, you know…. you need to be checked. Go the GP, they'll ***do everything!*** *This may because they haven't been seen for the last fifteen-twenty years by a doctor for many reasons (sic).*

The nurses had their own solutions to offer regarding these problems:

Participant (nurse): We've talked a lot in the London TB nurses group and put a proposal forward too that we should be looking at getting more 'one- stop shops' so people come in and get their treatment sorted out, get their social services sorted out, get advice about immigration, asylum you know with one service rather than coming to us presenting with all these problems and then were shopping around'(sic)

The nurses found it particularly hard, and even stressful, and they often felt guilty that they were unable to meet the needs of their patients, or even begin to address what was a priority for the patient.

3.53 Time restraints

Time limitations were seen as problematic for both doctors and nurses who were involved in the treatment of refugee groups and patients with TB, when it came to assessing the often complex needs of refugee and asylum seekers. Coupled with language difficulties, ten minutes can be grossly inadequate for health assessments for both GPs and patients. Refugees and asylum seekers have often experienced traumatic situations in their homelands, and these experiences are bound to influence the nature of health consultations with GPs and nurses. However, participants felt that it was possible to compensate for this by repeated visits:

Participant GP: We have ten minutes consultations, but we do have patients coming back, if things don't improve… they can come back to us. It's not as if they are waiting for an outpatient appointment or whatever… they can come back in a week if they haven't improved. So, they don't just get the one 10 minute slot at a time, they get quite a few slots of time.(sic)

The expectations of refugees about the role of health providers can be unrealistic, though TB is a complex disease, which affect all areas of a person's life. It was acknowledged that more time was required for these consultations in order to better meet these needs, some of which can be diverse and extremely challenging.

Participant GP: 'You can have lots of other problems…… and then some of them have terrific stories from the past….. you get a feel for what they've been through otherwise you don't know where you're going to begin and…there's all sort of things.. A girl who came from Africa who's pregnant…who was raped…well probably this is HIV…before you've even said hello… so you've got a lot of contentious issues to start with…and you've only got ten minutes, there's an awful lot of things to take on board.'(sic)

The nurses expressed similar views:

Yes, and that's really interesting to hear because sometimes, we really feel a bit like, you're ***expected to sort of help in every aspect****, and of course we want to, it's just that it's difficult to know the best, and to say this is not my remit…. I think it highlights as well some of the cultural expectations and the cultural differences and sometimes, how people react to news or how they react to their disease or how they interact with us,. Sometimes it can cause problems and that can be a bit of a barrier….(sic)*

The general feeling from GPs and nurses was that centralising services to provide a more holistic approach to assessment of both health and social care needs would improve access opportunities for patients and encourage attendance and adherence to treatment. The current fragmentation of services was identified as a major barrier to successful treatment and case finding in Brent.

3.54 Cultural competence

Cultural competence describe a set of behaviours, skills and attitudes that enable health professionals to meet the needs of ethnically diverse groups appropriately and with understanding regarding cultural differences(107;108). Culturally competent health care has emerged as a legitimate concern with the growing recognition that behaviours, beliefs and lifestyle, can profoundly affect health outcomes (107). Appreciation of such differences is necessary in order to prevent intentional or

unintentional discrimination and adherence to stereotypes that result from making assumptions about other cultures(92). Improved insight into cultural differences can encourage better design of services that are more sensitive to the particular needs of certain groups. More specifically, cultural competence describes a set of skills that 'maximise sensitivity and minimize insensitivity in the service of culturally diverse communities' and incorporates self-awareness and respect for others, as an approach to the healthcare relationship(92).There is no clear consensus or one single definition of cultural competence and the literature describes this concept at both an individual and a whole systems level. In simplistic terms the primary focus of culturally competent care is being able to provide health interventions in the appropriate language of the individual or community(107). At a more complex level however, cultural competence can be viewed as the organisation of culturally sensitive procedure, policy and resources that prevent institutional racism and allow equal access to all sections of the community regardless of background(92). Culturally competent care is therefore increasingly being viewed as a component to 'quality' care although can be difficult to measure(109;110).

We wanted to know whether doctors and nurses felt prepared in terms of their knowledge and skills to address and understand some of the cultural issues that emerged during their consultations and whether they were confident in responding to these concerns. Some participants reported that they lacked confidence when dealing with cultural issues that might interfere with the patient's care. It was recognised, for instance, that women from some cultures might have reservations about being examined by a male doctor. This was not considered a problem but needed to be held in mind in case a female doctor was not available.

Refugees may not attend their appointments and ladies who don't want to be examined by male doctor, who sometimes may not be available (GP)(sic)

However, it is also likely that women from a broad range of cultures may agree that it is more acceptable to be examined by a same sex doctor and this is not necessarily a reflection of 'culture' *per se* but could simply reflect personal individual choice.

The nurses generally felt confident in dealing with cultural difference among and between groups and did not think that any special knowledge or skill was responsible

for the development of cultural competence. Interestingly, one nurse reported that it was more important to possess the characteristics of openness and tolerance toward patients and that an understanding of shared characteristics was more important than being able to understand people's differences. The following excerpt from the nurse specialist in-depth interview makes an important point:

Nurse: Yeah, and it can be difficult for other people who haven't (had a lot of experience) and I think you have to be a fairly open sort of person because you know, if you had too many….set ideas then it would be very difficult I don't think you'd last very long.

Nurse: (giving example of culture influencing behaviour): … it's all been very odd and there are certain things with her (the patient) and things she's said that suggest she's not…….she's probably in an arranged marriage and you know not able to... whether she's being a bit….oppressed! (laughs) you know, it's difficult, you know, I mean obviously there is something going on but it could be just who knows? There is concern because obviously she has TB again of whether she took her treatment properly before and her nurse sort of has got concerns about the family and dynamics and whether that affects her treatment and all that sort of thing. But it's also you don't, we talked about it and batted ideas around but it's also whether we're sort of feeding in to cultural stereotypes, of you know the oppressed Indian woman, you know in a arranged marriage and all that sometimes……..

Researcher: Or whether they are just human issues…

Nurse: Exactly! Whether it's just family dynamics is a bit can be a bit, in many families, regardless of where they are from

Researcher: That's a really interesting point actually, I don't think anybody has ever said that, that the separation we talk about in culture, may not exist at all…you know, it's just a human commonality that people have…or difference…it doesn't necessarily mean it has to be cultural difference…

Nurse: No, that's right

Yeah! You know. I think there is something about people's personality, whether you know, not that anybody gets it right all the time or doesn't have conflicts or anything…I think its more about being open and I think it's about what we said that actually, ……where does culture and where does humanity sort of merge and actually….we're all fairly similar…..Laughter

Specific cultural customs were talked about as being significant to the health and wellbeing of some at risk communities. The Somali group and the GPs talked about Qat chewing in some African communities as being detrimental to health and possibly contributing to the spread of infection. The concern regarding Qat chewing related specifically to the circumstances in which the activity took place and how this might affect the general health and well-being of the entire family. A GP participant told us:

… It's a big problem and something that maybe a lot of GPs are familiar with…this is what is called Qat within the Somali communities. Yes, it is a very strange kind of drug…I call it a drug because, I…see people suffering, especially in this country.…it's a cultural thing. In Africa people have own businesses, or their own jobs. When they finish work, they sit down and they chew the Qat…and they don't like eating it in their own homes. You can go to like a pub. It is like social gathering …Over here it's a bit different… they smoke in the same room, where the rest of the family and the kids use. (sic)

Whether or not there is a physiological reason why the taking of Qat may influence Tuberculosis susceptibility, the time spent together in crowded rooms where an index case may be present could well provide the opportunity for greater exposure to the Tuberculosis bacillus and therefore present a greater risk of infection.

3.55 Immigration laws and regulation

Some of the participants felt that they did not know or were unable to keep up with immigration regulation with regard to health services entitlements. However, it was reported that some surgery practice managers tried to update themselves on the legal requirements. Doctors' receptionists were also educated in basic immigration laws as they were often the first point of contact for patients. It was felt that it was generally difficult to obtain a coherent set of regulations from anywhere. None of the

participants claimed that they excluded refugees from registering with their surgery, as long as they could show them the appropriate documents:

Participant GP: As doctors .....if we start getting too particular about things, they will either go away from us, they won't get the healthcare they need, Plus… it jeopardises the thing right from the beginning; first thing is them getting in the door as it were'(sic)

A nurse noted the potential seriousness of losing individuals through fear of what may happen, if information is disclosed about immigration status:

Nurse: And we ask about their immigration status, which can seem very threatening, you know, why are you asking me that, why do you need to know?! And for us, it's more about assessing their risk and their treatment and whether there are factors that will impact on whether they can take their medicines and that is a big factor… and if they're going to go underground and you're not going to be able to trace them then that's a big problem, and you know, I've lost people….(sic)

Earlier, I reported how the doctors resented being involved in assessing a person's entitlement to healthcare in relation to their immigration status and how they felt that this sometimes resulted in them being viewed as the police. The nurse explains above that this questioning in the health context relates helps identify those who are at high risk of TB by virtue of their recent immigrant status. It is likely that this relationship is not adequately explained by health professionals, which may potentially leave the impression that health workers have a regulatory function in terms of immigration law.

3.56 Building an explanatory model of the experience of Tuberculosis in Brent.

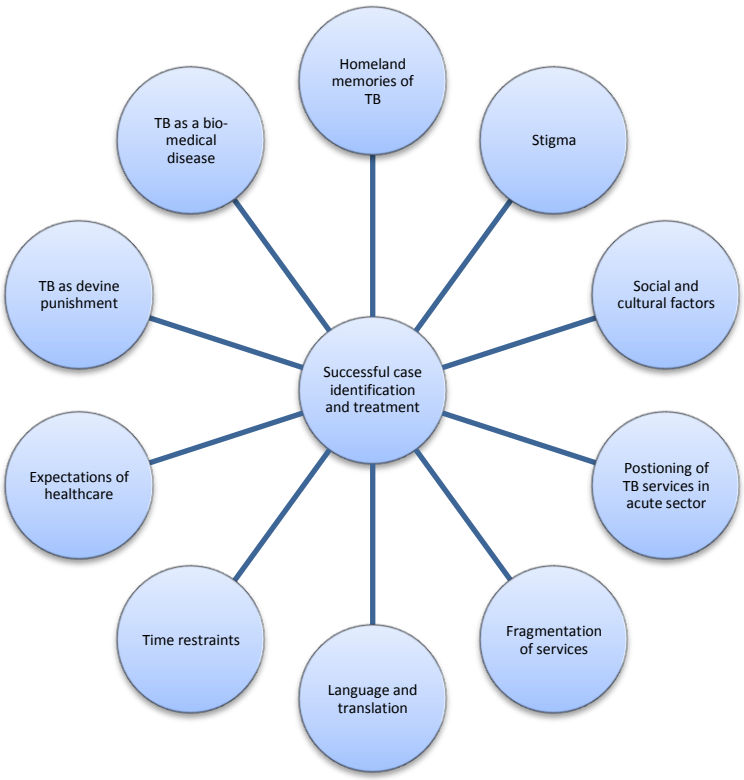
This project has provided and in- depth insight into the community experience and the knowledge and perceptions of TB among high risk groups in London as well as exploring the impact of cultural and social factors through in-depth discussions with 'at risk' groups. Research questions 1 and 2 particularly have addressed these elements through focus group discussions. *Ie 'how might community experience influence disease prevalence of TB among refugees, asylum seekers and homeless*

people in Brent and: are there cultural and social factors in different refugee communities and do these affect people's willingness to be treated or seek help? For the community groups, themes were identified through an inductive analysis of the data that encapsulated the common themes and the strongest elements of the stories. These related to history and memory of home countries, stigma, TB as divine punishment, social and cultural factors and TB as bio-medical disease.

The inclusion of the health professional groups provided an essential perspective in terms of describing some of the challenges faced by health professionals treating Tuberculosis within the community. Research questions 3 and 4 were answered by these groups: i.e., *what are the barriers that may affect the uptake and service delivery to asylum seekers, refugees and homeless people* and *what are the institutional gaps in prevention, detection, notification, diagnosis, treatment and follow-up?* Interview schedules were designed to tease out these points and a rich description followed regarding the health care experience. Health professionals reported the problems and complexities of language and translation, time restraints, fragmentation of services, the financial limitations faced by many with Tuberculosis, expectations of health care and the current system of referral for TB patients as all providing challenges to successful case identification and treatment. Therefore, on the one hand the community view provides an insight into what it must be like to deal with a diagnosis of TB in the community and the complexities around dealing with it, in terms of one's own personal history, current situation, knowledge and beliefs and on the other, the experience of those who must find and treat Tuberculosis cases. And finally question 5 addressed knowledge of Tuberculosis, in order to gain insight into the level of understanding that existed about the condition within the target groups. What remains is to define how these perspectives, beliefs and perceptions potentially impact on the continued *prevalence* of TB in Brent. It is possible through bringing together both points of view from this research to construct an explanatory model that describes how this might be the case and proposes ways that successful case identification and treatment may be inhibited by their presence.

Figure 12 explains provides an overview of the model incorporating all the themes identified through this study and proposes their potential impact on case identification and treatment.

Figure 12: Explanatory model of the experience of TB in Brent



3.57 Discussion and conclusion

This research has demonstrated that there are significant factors that relate to the community perception, knowledge of disease, elements of social life and service configuration in Brent that have the potential to influence both prevalence of disease (through possible avoidance of health services) and successful treatment (through inappropriate configuration of services). All of the elements identified can be viewed as barriers to successful treatment and case identification to a greater or lesser degree except perhaps, the perception of Tuberculosis as a bio-medical condition. Belief in bio-medicine i.e. the belief that TB is caused by a pathogen that can be treated with modern medicine and drugs could potentially *facilitate* case finding and adherence to treatment, as a belief in medicine potentially supports the motivation to seek help and be treated by a doctor rather than a traditional healer for example. This research has demonstrated that in some groups though, a belief in bio-medicine can co-exist with other causal beliefs of disease such as divine punishment for wrong doing. These co-existing beliefs therefore could confuse the priority in which people seek help. It is possible for example that those with co –existing beliefs regarding bio-medicine and

divine punishment might seek the help of a traditional healer or a religious leader first and this may delay diagnosis and pose an infectious risk to the surrounding community.

Additional factors were discussed by GPs as being important to the continued prevalence of Tuberculosis. There was a belief expressed that the number of TB cases in Brent was likely to be much higher than official statistics show. This commonly held belief came from the suspicion that those at risk or who were experiencing symptoms of disease did not always seek help from health workers. Finding and treating latent cases was discussed as a missed opportunity in TB management in Brent and could provide an effective response to the delay in seeking help as such programmes would prevent potential activation later on. The location of health services was seen as a significant barrier to case identification and treatment. The GPs who took part in this research acknowledged that most of the clinical care of TB patients occurs within the acute sector, in Chest Clinics, to which people are referred by their GPs, often on the basis of clinical suspicion. TB nurses are then usually responsible for much of the care and follow-up of TB patients and provide a vital role in supporting patients in the community. Some participants felt that the provision of TB care within the acute services was well placed while others expressed a desire to be more involved in the care of those with TB. GPs felt that once their patients were diagnosed they were no longer involved in their care or able to prescribe treatment, even though they may be better placed to do so. The community groups expressed a view that being seen at such clinics was stigmatising and therefore best avoided. The provision for the specialist services within Chest Clinics in secondary care may therefore not be the ideal situation for both patients and health providers.

When asked whether GPs and nurses possessed the right skills, knowledge and resources to diagnose the condition, most felt confident that they could, however, some felt that they would have difficulty diagnosing non-pulmonary TB. This was primarily because its presentation is often complicated and less obvious and, generally, the resources required to clearly identify non pulmonary TB do not exist within primary care. The requirement to refer the patient on to secondary care can be frustrating.

Additional frustrations from health professionals included difficulties in treating refugees. The language problems, time restraints and problems with referral that often resulted in patients becoming lost in the system enhanced the complexity and difficulty around consultation with their patients. Very few studies have examined these problems. One study recently examined refugee health problems in general practice in London but no studies have explored perceptions of Tuberculosis and focused specifically on the refugee experience(111). More work is needed to increase understanding in this area.

3.58 Health services

General practitioners in particular, felt that they could contribute more to the treatment of Tuberculosis in Brent, and that the current separation between primary care and acute services sometimes provided a barrier to patients who were referred to chest clinics in hospitals. For the patient, this often meant extra expense for travelling to and fro and some communities reported their reluctance in attending these clinics as a result of stigma. Removal of TB services from hospitals into the communities at risk would help provide a more seamless service with less fragmentation of service provision for poor communities who often experience a number of health problems that all require attention and that chest clinics are not set up to address. Health professionals also felt unable to provide all the care that was expected and some reported feeling guilty that they were not able to meet all the complex needs experienced by this group.

3.58.1 Culture as a factor in the community perception of Tuberculosis

The research also sought to understand the impact of culture and how cultural differences may also influence health belief and how cultural competence among health providers and the relative confidence among these groups could either help or hinder successful treatment.

I began this study with a preconception that a person's culture would be a strong factor in influencing beliefs and behaviours about Tuberculosis. In the end this assumption was difficult to realise or qualify. Some examples of 'cultural' differences were provided that were specific to certain groups such as Khat chewing in Somali men, but cultural examples were not heavily reflected in the other stories.

Nevertheless, there are likely to be shared beliefs and experiences within immigrant communities that inform a new way of life and a new way of being for those who have come from very different societies where the mores and values are in stark contrast to our own. For these people, adjustment and adaptation are key in their new society, and this requirement can be a powerful force in determining how people behave and the relationships they develop with others(54). It is the new culture of the immigrant and the pressures of such an adjustment that must be considered by health workers when planning and delivering services. For instance, the prospect of being ostracised or isolated by their peers in the new setting would be extremely damaging to individuals who require the support of their fellow people in order to survive. Research has previously demonstrated a strong commitment from refugee communities to make new relationships and to adjust to the host society(54). Isolation as a result of stigma for example, would be best avoided. It is both the 'culture' of the old and the reality of the new that determine this fact.

Other cultural elements that were explored related to what different groups believed caused Tuberculosis. The Somali group held a belief that this was punishment from God for wrong doing. It would not be illogical to report this finding as a cultural determinant of behaviour. But would this be accurate? The view of divine retribution is expressed in all kinds of ways in many societies, particularly devout ones. Perhaps it is just a human response to what feels like injustice. A recent study in cancer patients in the Netherlands has shown that patients experience guilt associated with their disease. This was more strongly reflected in those with religious belief(112). Although not discussed directly in the context of divine punishment, the association of guilt, forgiveness and punishment are closely related conceptually. This phenomenon may therefore be more a product of spiritual orientation rather than a reflection of cultural belief. This would be an important area of future study as regardless of its origin it appears to be significant in defining a response to illness.

This research supports the work of others that have shown that, in vulnerable communities, the stigma and taboo of Tuberculosis exists and makes individuals reluctant to be identified as having the disease(44;47;113); although few studies have focused on the perceptions of refugee communities specifically. TB is known to be a stigmatising disease across the globe, although reasons for this stigma may differ

from place to place(114). The results of this study suggest that there may be a 'double stigma' for refugee communities in their new societies. One dimension of this relates to their low status as a refugee and the other to acquiring a stigmatising condition. Stigma very much depends on the local context as well as the historical condition of the community in question. This research has demonstrated how past experience might influence this dimension of stigma. It has also demonstrated how elements of knowledge, belief about the origins of disease and social factors all overlap to form an explanatory model that provides a descriptive account of some of the difficulties and barriers to treatment of Tuberculosis in Brent from both the community and the health providers perspective.

3.59 Limitations of this study

The strength of this study lies in the positioning of the investigators as insiders of the community enabling the discussion from the respondents with the professionals as outsiders analysing the stories. However, it is important to consider the possible negative effect of this positioning in the potential to also inhibit the stories(116). It is possible that the respondents may have been concerned about revealing thoughts and experiences that could be harshly judged by their peers. It is difficult to know whether this was a factor in this study. As an outsider, analysing the responses it was sometimes frustrating as the group leaders did not follow the stories through or ask questions at the points in the responses where I felt it was relevant to do so, or where a deeper understanding of an important issue could have been gained.

3.60 Data quality

Although the group leaders were given instructions about how to run the groups and strict guidance on the management of the data, some of the transcripts we received were not transcribed verbatim and we were presented with a summary of the discussion rather than a transcribed version. This limited our relationship with the data as it was not presented in its raw form, but was more an interpretation of the discussion translated from one language into another (English). It was therefore difficult to know whose 'voice' was speaking, i.e. that of the group facilitator or the respondents. This presented us with a conceptual gap, as the stories of some of the groups had essentially passed through two filters before we were able to see them.

One filter related to the translation aspects and the inaccuracies and gaps that may have existed in relation to conceptual equivalence and translator skill. The second filter was the interpretive schemes of the group leaders who reported the findings of the conversations rather than verbatim transcripts. However, this in some cases provided interesting insights into the facilitators' view. For example, one of the group leaders was a qualified doctor in his homeland and his transcription was surprisingly fluent (or not so) in terms of knowledge of treatment and infectious diseases in general. The transcript was not at all what the respondents actually said but rather a doctor's interpretation of what people ought to say. We cannot say for certain, but we were surprised that members of his group knew the names of Tuberculosis medication and streptomycin injections as a therapy. The other effect that may have been at play with the 'insider method' that we adopted was that the group leaders may have been motivated to portray their communities in a positive light. This could have lent itself to a selective portrayal of the conversations in order that they were presented as knowledgeable sophisticated accounts. Given that their employment as refugee group leaders provides some evidence of a passionate connection with the groups, it is possible that some bias resulted in the presentation of the data as a result. Many of the group leaders were themselves once refugees and would undoubtedly have had strong opinions on the topics being discussed.

3.61 Translation

Although we undertook the focus groups in the native language of the respondents, we did not use the method of blind 'back translation' suggested by other workers(92). This is a process that involves *'two bilingual, bicultural interpreters, A and B. A first translates the material into the language that A is most competent; B then translates A's translation back into the source language in which B is more competent. The two versions are then compared and corrected'*(115) Our scheme resulted in A translating the material from a language in which they were more competent into one in which they were less competent with no quality assurance in the back translation offered by another translator. We were, therefore, unable to determine whether the themes that were derived from the data and fed back for responder validation travelled accurately through the back translation process as no second translator was present. We did not,

however, receive any complaint that any of the respondents disagreed with our analysis.

There is also a possible gap that can occur through a lack of conceptual equivalence that may exist from one language to another. One may even argue that there is a gap between the description in language and the experience itself(115;117;118) or that conversely, Derrida's assertion ' *il n'y a pas de hors-texte'* i.e., there is nothing beyond the text at all, suggesting that our experience of the world and the language we use to express it are inseparable. This reflects a rather extreme view, yet raises a legitimate point in that access to our understanding of the world or the lived experience of those who speak languages that do not closely reflect our own in meaning, structure and origin could leave us at a serious disadvantage as researchers. Beyond the text, however, there is yet another conceptual 'gap' that can appear. That is, first the ability of the respondent to express their feelings and experience clearly and articulately in their own language, and secondly the nuances and subtleties that are lost from the spoken word when they are transcribed into text(118).

3.62 Reflexivity

As discussed in the beginning of this work, the biography of the researcher in qualitative research brings another dimension to the analysis that can potentially bias or enrich the findings of inquiry. For this reason it is vital that preconceptions, expectations and personal history are understood in light of reported findings in this kind of work. The fact that the insider's view may be very different from the outsider's observation does not apparently exclude understanding. A combination of both perspective can provide a 'third dimension' to the experience under scrutiny(119). In terms of this project and the contribution of the research team and how our various positions may have shaped the analysis, my experience as a nurse specialist and of researching attitudes to Tuberculosis in the past meant that I was certainly looking to find elements of my previous experience to support my understanding on the subject. Dr Mahmoud was a refugee, and similarly, had strong opinions about health in refugee communities. One theme I was not surprised to see emerging within the Somali group was the belief that God was responsible for Tuberculosis in individuals. I had seen this before. However, what I felt was new and unique to my understanding of this issue in the context of this study was the idea

that this did not necessarily exclude the simultaneous possibility of Tuberculosis as a biomedical disease. The idea of divine punishment is something that is felt as an existential reaction to extreme experience rather than a rational belief about the cause of disease. This apparent contradiction was reflected in the answers that people provided us when we asked what caused Tuberculosis. Even those that held the belief of divine punishment reported that they knew that Tuberculosis was caused by bacteria. This challenged my own view about the role of culture in determining health belief and provides a caution against essentialism.

It would have strengthened this study if we had asked the group workers to make explicit their positions in terms of their experiences and beliefs in the form of field notes(79;83). As refugee workers they were well motivated to take part in the study, but this motivation may have equally influenced the way in which they approached or asked the questions and even perhaps what they remembered to document. In qualitative work *'preconceptions are not the same as bias, unless the researcher fails to mention them'*(78). A more systematic approach to documenting these preconceptions would have strengthened this study and the final analysis.

3.63 Recommendations and implications for clinical practice and further research

There is no doubt that the successful treatment of Tuberculosis is complex and difficult. There are many reasons why this should be so. First of all, Tuberculosis is a disease that affects mainly poor developing and third world countries. Many people from these countries migrate and resettle in capital cities across the globe. Yet migration alone does not explain the persistence of TB however convenient this might be in supporting the political perspectives of some. There is a complex interplay of social and biomedical factors present in both the environment and in the biology of the host that come together to form 'the recipe' for TB infection and transmission. The appropriate combination of factors (the ingredients), are more likely to be present in poor, underprivileged communities across the globe. Advances in medicine are largely determined by industry, economic forces and the motivation behind solving medical concerns driven by political policy about social concerns. Why should global pharmaceutical conglomerates concern themselves with developing better treatments for Tuberculosis in the developing world? Who will pay for it and is there likely to be

adequate financial return on such technologies? Even if the technologies are produced can they be successfully employed in countries that lack the required infrastructure to manage them? These questions are important because the fact that there are no real answers partially explains why we have not progressed very far. For example, the antibiotics for treating Tuberculosis have been in existence since the 1940s with the discovery of streptomycin which in some places is still used. There has been very little refinement to the treatments to date. The course of treatment for Tuberculosis remains long and has unpleasant side-effects. There have been some important advancement however in diagnostic technologies; the development of interferon gamma assays for example has important potential in preventing active infection by identifying those with latent disease. Unfortunately, these assays are rarely used in high prevalent countries because they are expensive or the required infrastructure to run them does not exist.

Secondly, there is a need to consider the global nature of TB and the fact that infectious disease does not respect boundaries and borders. This makes local management difficult because local clinicians are unable to address global problems. Therefore, a global political commitment is needed to address the management of Tuberculosis; a fact recognised and articulated by the World Health Organisation in its 'Stop TB' programme. But where is the funding for these expensive and difficult programmes? Where is the money for the research? The investment for Tuberculosis research programmes is minuscule, when compared with other infectious diseases programmes such as HIV. One might be inclined to ask why? I would argue that the principal reason for this disparity and inequality is related to whom the diseases affect, and therefore who then champions the cause and whether these people are important enough to care about. During the 1980s in the UK and America when HIV and AIDS started to affect intelligent, middleclass white people, high profile celebrities ' came out', in order to reduce the stigma and fear around HIV and AIDS. It quickly became a high priority for medical research. There were campaigns, advertisements and even concerts all to raise awareness and reduce the stigma around the condition at the time. Princess Diana of Wales was famously filmed holding the hand of an AIDS patient in London and this was televised and discussed as a significant challenge to public opinion and the fear that arose from misconceptions about disease transmission. There was a viable commercial market for new

treatments and revenue for these technologies was not impeded by poor infrastructure or lack of political commitment. The industry response to the emergence of HIV saw the development of new antiretroviral treatments and medically, it became a prestigious area of study not because people in Africa were dying from it, but because high profile middle class westerners were.

We have learned from the AIDS experience that investment in dispelling myths and education for the public and health professionals works in both prevention and successful treatment. It should be possible to replicate this learning and transfer it to the Tuberculosis problem. Yet sadly, it has not been prioritised in the same way because it is not perceived to affect anyone important. Those who are 'important' and could act as champions have not come forward. Could this be because the stigma is so malignant and far reaching?

This study has shown that stigma is damaging and has the potential to isolate and encourage concealment of disease and avoidance of health care providers. There is a need for more education to dispel social myths about Tuberculosis but I am unclear how this should best be executed and achieved. The social identity of those affected is also important. The profile of refuges in London is not very positive. Campaigns would be needed to address this problem too, relating to the potential contribution of refugees to society, in order to raise the status of such groups so that they become important enough for people to care.

During this research I met numerous nurses, doctors and lawyers who were refugees and were unable to work in the UK, but were keen to challenge the stereotype of refugee communities. As insiders of their communities, these people could work in partnership with health providers to inform them about their educational requirements and in some cases, it may be possible to establish programmes for education working together with refugee communities. Liaison with religious leaders and encouraging their involvement in Tuberculosis education programmes would also be helpful in addressing particular perceptions of stigma among the Somali community given the status of such leaders and the importance of religion to Somali life.

Given the energy and enthusiasm of the people who took part in this research and also the refugee organisations who volunteered to run the focus groups, there could be a

very important role for refugee centres in the provision of health care for refugees. This should be considered and if successful, translated to other areas of the country that are home to refugee communities. This could be particularly important in reaching the homeless communities, who the professional groups report are difficult to follow-up. Find and treat clinics could be established in refugee and community centres and greater use of the Quantiferon test as a screening tool for latent and active disease as opposed to the Tuberculin skin test could simplify screening programmes and allow greater 'outreach' work to take place locally. The global problems around TB management remain challenging.

Some of the health workers reported that they felt they were often classified as 'the authorities', and rather than health workers being viewed as helpful, they were sometimes conceptualised as those who policed or institutionalised those who were ill. This confusion often resulted from health providers questioning of immigration status. Education is needed among at risk communities regarding risk factors for Tuberculosis and why these questions are asked by health providers during their consultations.

Thought needs to be given to the structure of health services to address the fragmentation of health care discussed by the health workers. A 'one stop shop' model that includes social services, housing advice and social care facilities would address some of these issues and may provide a more economical health industry model.

The success of this project was surprising, given the stigma surrounding Tuberculosis, yet we were unable to speak to patients who were suffering from the disease and none agreed to take part. The approach taken to the positioning of researchers in the field is recognised as a necessary strategy and usually attempts of outsiders to infiltrate such groups often fail(115). My distance from the field in terms of language, experience and culture may have coloured my analysis, although no challenges were offered by the respondents to the themes that were collated from the community stories. Successful engagement lay partly in the fact that the community groups themselves led the discussion groups and this provided a sense of ownership and empowerment for them. The facilitators, as insiders of their communities, were able to speak the language and access people's stories in a way that we believe would

not have been possible if health workers had led the project. The communities expressed their enjoyment of having taken part, and were motivated by doing something for their communities regarding public health problems. One focus group had to turn away members who wished to take part due to a lack of crèche facilities.

In summary the following recommendations for clinical practice have emerged from this research:

- Education programmes are needed to challenge and dispel stigma among at risk groups using high profile members of target communities.

- Find and treat programmes should be established within the communities and refugee centres and a similar model of health provision should be utilised in terms of the positioning of health workers as is reflected in this research. I.e., the community members, and insiders of the groups could be employed as TB health workers providing education to community members and acting as bridges between the community and the health providers in order to mitigate any perceptions that may exist of health workers as 'authorities'.

- One stop shops should be set-up to deal with the host of problems often faced by those with TB in order to offer an integrated service that provides social as well as medical support and treatment. This would better meet the complex needs of these patients and there would be less need for them to travel to different sites for different aspects of their care; a requirement which is often difficult for those who have very little financial resources to begin with.

- The placement of TB services outside of acute health care in general should be considered with greater involvement of GPs, who given the correct resources, skills and knowledge would be well able to support treatment regimes for active TB cases.

- Future research should focus on reducing the negative impact of the themes identified by this research and described in figure 12. Increased understanding regarding the impact of any of the themes would also provide a deeper insight into how perceptions and experience might affect the health seeking behaviours of at risk groups. Greater understanding regarding the perceived

relationship between illness in general and the concept of divine punishment would be very enlightening. The exploration of this relationship within different disease groups and communities would be recommended in order to explore the concepts within the wider social and cultural context of human experience.

- New models of health care provision should also be fully evaluated.

3.64 Summary

This chapter sought to answer the questions of how community experience in a high risk population might influence disease prevalence through perception and knowledge of disease and how these perceptions may potentially influence health seeking behaviour. We have seen that stigma, memory of homeland experience, social and cultural factors, the belief of divine punishment can colour the way people respond to disease and potentially influence willingness to seek help and be treated. Health professionals reported their experience with language and translation challenges that prevented meaningful discussion with patients and described how the expectations of healthcare from migrant groups sometimes outweighed or were not congruent with what they were able to deliver.

These findings are the result of considering the human element of inner city living and how the realities of modern life and perceptions of it, in a large capital city influence responses to Tuberculosis. The city however, has a physical presence reflected in the built environment and this too can influence health risks as described in earlier chapters of this thesis. The experience of city life, as determined by its people and the influence of the built environment both contribute to population health outcomes. In the next chapter, I explore the contribution of sunlight exposure on Vitamin D status of a Tuberculosis group living in London. The relevance of Vitamin D status to Tuberculosis risk and city life will be explored.

3.65 Acknowledgement

I feel privileged to have undertaken this work and to have been allowed such a rare human insight into the community life, beliefs and opinion of the people of Brent. I am especially grateful to Dr Amna Mahmoud, my co-researcher, herself once a refugee from Sudan, who has dedicated her professional life to improving the health and wellbeing of refugee groups in London. The results of this study were first presented as an oral paper at the International Nursing Research Conference in 2007, the CRNA in 2007 and published as a public health report by the Brent Refugee Forum.

4 Chapter 4: A study to determine the contribution of sunlight to Vitamin D deficiency in a Tuberculosis population.

4.1 Introduction

In the previous chapter we have seen that there are many barriers to successful case-finding and treatment of Tuberculosis in a large city environment and some of these are socially determined and inhibited by the prevailing stigma associated with the condition. We have seen that these obstacles are powerful in shaping the possibility of effective treatment and that the appropriate configuration of health services is fundamental to success. These factors require understanding and sensitive appreciation. We have shown how the community response to Tuberculosis is one aspect of understanding the complexity of the Tuberculosis problem because it influences behaviour and belief.

In the brief history at the start of this thesis I described how urban living was instrumental in shaping public health in the past. This is, of course still the case today. Interaction with the environment remains an important variable in human health, infectious disease and, indeed, survival. As well as crowding and population density as significant factors in the spread of infectious disease, host factors may also play a part, especially those that depend upon the environment for their acquisition.

I have described the problem of Tuberculosis in London and its increasing prevalence as a public health problem. Regardless of improved living conditions, Tuberculosis has remained a significant public health concern. London remains the hub of Tuberculosis in the UK. Additionally, many of the risk factors that contribute to the likelihood of developing disease are experienced within the urban environment and include socially determined elements of risk, such as overcrowding, homelessness and poverty(8).

I would now like to move on to explore how city life may influence the Tuberculosis story in a different way. City living has many challenges and these include the physical contribution of the built environment, indoor lifestyles, public travel, exposure to allergens, atomised microbes in water, and indoor plumbing and air-conditioning to name but a few. For many years health researchers noted and

recorded the phenomenon of '*sick building syndrome',* in which large corporate work places were seen as significant in the health of the workforce(120;121). The World Health Organisation produced a report in 1983 describing the problem and its effects and concluded that most of these non-specific health related complaints associated with Sick building syndrome, were due to poor ventilation and air quality, demonstrating the impact of the built environment on human health in modern times(122).

In this chapter I describe a problematic clinical experiment that was designed to answer the question of whether Vitamin D deficiency in Tuberculosis patients was a result of lack of sunlight. I observed the exposure behaviour of Tuberculosis patients and their contacts over a period of time. I will describe why the question is important and the challenges that I faced in realising this experiment.

4.2 Sunlight and Tuberculosis-Literature review

Although the cause of Tuberculosis is now well understood, not everyone who is exposed becomes infected or develops disease. It is therefore important that the relative contributions of other factors involved are made explicit. One such factor that has historical resonance in the Tuberculosis story is sunlight and its use in the treatment of Tuberculosis. Prior to my experiment I designed a search strategy of published work that would describe research in this field.

4.3 Search methods for identification of studies

I searched MEDLINE and CINHAL databases from their start dates. I also searched reference lists of published studies. I did not hand search individual journals. All databases were searched from their start date to 2005, prior to starting the study. A further search was repeated using the same search strategy prior to writing this thesis in 2011. There were no limitations by language.

The search strategy comprised three overlapping concepts:

1) Tuberculosis

AND

2) Vitamin D deficiency/Colecalciferol

AND

3) Sunlight

I used the search strategy presented in Appendix 6. The search revealed 24 papers that related directly and were relevant to the subject area.

4.4 Tuberculosis and sunlight

Exposure to sunlight for the treatment of Tuberculosis first became fashionable in the mid 1800s with the opening of the first sanatorium in 1859 in Germany. Later Finsen conducted a number of uncontrolled clinical experiments using optical lenses for the treatment of small pox and *Lupus Vulgaris* 1903(123). Finsen intensified the exposure of his subjects to sunlight using these filters to harness the energy of sunlight as he strongly believed in the healing properties of light. In these experiments he observed that these 'chemical rays' completely cured small pox vesicles and left no scars(124). Later, he refined his technique achieving positive results for the treatment of *Lupus Vulgaris.* 56% of 800 patients being treated by Finsen's light therapy between 1895 and 1902 claimed a complete response to treatment(125). Finsen was awarded the Nobel Prize for Medicine and Physiology for his work, although, at the time the mechanism for success using light therapy in these cases was not well understood. Recent workers have sought to elucidate more precisely the effective mechanism of this early work by recreating Finsen's treatments using similar glass lenses(125). Although Finsen himself postulated that light was responsible for the destruction of microorganisms, accurate measurement of wavelength was not possible at the time. Since then, there has been considerable progress in describing the properties of ultra-violet radiation (UVR) and its effects on biological systems as well as its germicidal potential(3)

4.5 Tuberculosis, vitamin D and sunlight

Recently, there has been resurgence in interest in the contribution of Vitamin D status to human health, including Tuberculosis, with one large clinical trial assessing the possible contribution of supplementation in this group(126). Vitamin D is synthesised in the skin when exposed to high energy UVR in the UVB wavelength. Global epidemiological data suggests a positive correlation in the incidence of other chronic diseases including MS, IBS, cancer (colon, breast and prostate) and cardiovascular disease (127-132) with increasing northern latitude. This relationship is perhaps not unexpected, given the presence of the Vitamin D receptor for the active metabolite of Vitamin D, in many human tissues including breast, colon, brain and cardiac muscle, to name just a few(133;134).The principal variation in global conditions that defines Vitamin D status in populations relates to sunlight exposure as a function of latitude. Researchers have, therefore, sought to measure the contribution of vitamin D status in relation to these conditions based upon the assumption that cutaneous sunlight exposure is principally the most important variable in Vitamin D status in humans. It is indeed often quoted that up to 90% of serum Vitamin D is a result of exposure to UVB(135). More often, it is stated that sunlight is principally the most important variable in vitamin D status in man(136;137).The referenced source of this evidence very often reports epidemiological studies conducted outside of the UK, and few studies report findings at an individual level(136;138).

It is well understood however, that Vitamin D status is mediated by UVR exposure in the general population(139;140). Seasonal variations in Vitamin D status have been reported that validate this finding(141). It has been observed that patients with active Tuberculosis tend to have lower levels of Vitamin D than healthy contacts in the UK(142;143). More puzzling, is the presence of Vitamin D deficiency in Tuberculosis patients in countries that experience intense and long year round sun exposure; including Africa and India(144-147). Moreover, it has been shown that healthy contacts with low Vitamin D status are more likely to develop active disease later on(147). In the UK it has been noted that recent migrants to the UK travelling from countries of high prevalence are at greater risk of developing active disease within the migrant setting, supporting a theory that lack of sunlight may be significant in the decline of Vitamin D levels and subsequent re-activation of disease(148-150). One study found that from a sample of 210 Tuberculosis patients 76% were deficient

and 56% had undetectable levels(150). These workers found no relationship with season or duration of stay in the UK, which would seem to contradict the sunlight exposure argument as the cause of Vitamin D deficiency in these patients(150). The theoretical relationship between lack of sunlight and Vitamin D deficiency is thought to result in re-activation of latent disease as a result of the immune-modulating effect of Vitamin D metabolites, a factor that have been more recently elucidated(151).

This relationship, however, remains theoretical as the cause of Vitamin D deficiency in those with Tuberculosis and only one study has estimated the sunlight exposure of Tuberculosis subjects using a questionnaire(152). Unfortunately, the use of such instruments can result in imprecise estimates of UV dose(153). It was, therefore, of value to explore the strength of this relationship in a detailed study of a discreet group of subjects to further understand the contribution of sunlight to vitamin D status in a TB population. It remains unclear whether Vitamin D deficiency in Tuberculosis patients is a cause of disease or a result of it and there is currently no known mechanism that can explain how this might occur(154). Further elucidation regarding the strength of this relationship may signify the likely direction of this correlation. Prior to reporting the experiment I shall provide an overview of factors that affect vitamin D production and its importance in the Tuberculosis story, and the complexities that arise when consideration is given to the accurate measurement of UVR in an inner city environment.

4.6 The contribution of sunlight and diet to Vitamin D status

The generation of Vitamin D is induced through a photochemical transformation of 7-dehydrocholesterol (7-DHC) to precholecalciferol (Pre Vitamin D_3) when exposed to high energy UVR in the range 290-315 nm (UVB)(140).There is then an immediate conversion of previtamin D_3 to Vitamin D_3 which, through isomerisation, is drawn into the capillaries in the skin by attachment to the Vitamin D receptor through which it enters the venous circulation. The contribution of diet to Vitamin D status is often reported in the literature ‘as minimal’, with most being made in the skin as a result of photosynthesis. It is reported that very few foods contain Vitamin D in any useful quantity, oily fish and fish liver oils being the main source. Small amounts also exist in egg yolks and liver(155). A recent study, however, showed that there is much less Vitamin D in commercially available foods than first reported, with traditional

sources of Vitamin D, such a salmon, having only 25% of the reported Vitamin D, in farmed products as opposed to wild fish. In the UK very few foods are supplemented with extra Vitamin D.

4.7 Sunlight and Tuberculosis notifications

Epidemiological research supports the hypothesis that notifications of TB in the UK rise at times of the year when serum vitamin D levels naturally fall at a population level(156;157). Vitamin D is photosynthesised in the human epidermis when it is exposed to UVB light, thus peak concentrations occur during the summer months when levels of ambient UV are high. When concentrations begin to decline in the winter months, it is thought that some individuals, who have already been infected with the pathogen, develop active disease as a result of the immune-suppressive effects of falling serum vitamin D. Notifications of TB increase in the summer months, especially in those with darker skins, and the delay in reporting can be explained by the time it will usually take for a person to develop symptoms and seek help. The seasonal pattern of TB notifications is contrary to the normal pattern of infectious respiratory disease, where prevalence increases in the winter months and declines in the summer months. This contradiction could be explained by the fact that Vitamin D levels in humans are largely a response of UVB exposure, little of which is available in the winter months in the UK.

4.8 Why is Vitamin D important to the TB story?

The importance of vitamin D to the human immune system in general has been previously described including the presence of the Vitamin D receptor in human inflammatory cells(158;159). Apposite functions include immunosuppressive and immune enhancing effects. Vitamin D is important in modulating macrophage and monocyte action, important first line defence mechanisms(160). Mycobacterium TB is an intracellular pathogen that inhabits the macrophage, thus reduced monocyte-macrophage function is thought to play a role in disease development(158). Each monocyte has been found to possess a receptor for calcitriol (1, 25-dihydroxyvitamin D_3), this being the most active metabolite of Vitamin D. Not only does the metabolite enhance the action of phagocytosis and granuloma formation but also it acts in synergy with γ interferon, to prevent the intracellular replication of MTB(161).

Vitamin D supplementation has demonstrated a statistically significant enhanced ability of whole blood to restrict growth of mycobacterium measured by BCG lux luminescence *in vitro* in healthy controls(162).

Deficiency in Vitamin D can impair the health of helper t cells and their subsequent expression of interleukin-2 and γ interferon and other cytokines that are central to antigen specific immune response of these cells(163). Additionally 1,25-dihydroxyvitamin D_3 has been shown to mediate expression of *cathelicidin (LL-37),* an antimicrobial peptide with significant action against intracellular M*ycobacterium Tuberculosis*(164).The human cathelicidin gene is a direct target of the vitamin D receptor and is up- regulated in cells by the active form of Vitamin D (1,25-dihydroxyvitamin D_3)(165).

4.9 Human interaction with the environment

The environment and our interaction with it can affect health outcomes. It has been found that in veiled Turkish women for instance, concentrations of serum Vitamin D were significantly lower than those wearing western style dress(166). Similar results have been demonstrated in veiled women in Denmark(167). Studies have described the peak times in the year when humans produce abundant Vitamin D. In North America, the most prolific production of Vitamin D_3 occurs between June and July when ambient high energy UVR is high. Other studies have sought to determine when seasonal photolysis begins and ends. One study showed that at 52° north, this began in April and ended in October. None of these studies examined people in their natural environments, but rather modelled predicted Vitamin D potential from bottled samples of 7-DHC solutions in borosilicate ampoules(168;168;169). In genuine samples of skin type 3, photolysis using the same experiment was shown to be considerably less than the bottled 7-HDC(170). This could have resulted from the fact that the skin samples that were used were discarded foreskins. Foreskin and genital skin in general contain more melanin than facial or forearm and hand skin, parts of the body that are commonly exposed to the sun. Yet data from these studies has enabled Chen et al to model the predicted capacity of this skin type to photolysise Vitamin D_3 at different latitudes on a monthly basis(168). Although theoretical, their study has illustrated the considerable variation in the ability of skin to produce Vitamin D_3 at different times in the year, depending on latitude and season. Other

factors such as zenith angle of the sun during the changing seasons and increasing latitude all affect the skin's ability to produce vitamin D(168). Atmospheric pollution, low level ozone and air pollutants produced by industrial activity and city traffic may also affect the predominance of available UVR(171). I explore this possibility in the next chapter of this thesis.

4.10 Melanin

Cutaneous exposure to UVB stimulates melanin production in the skin. This is what gives the skin the characteristic tan colour, sought by sun seekers. The amount and quantity of melanin present in the skin depends on the prevalence of melanocytes situated in the epidermal-dermal junction. The bodily distribution of these specialised cells has been shown to exist equally in all races. Melanocyte density is greater in facial skin and the genital region than the trunk and thigh(172). Although there is some inherent relationship in the amount of melanocytes present in skin, sun exposure is also a determining factor in their increased presence. Melanin is supremely effective as a sunscreen as it prevents damage to the deeper layers of the skin by absorbing UVR. This prevents penetration to the *stratum basale* and *stratum spinosum*, where the greatest concentration of 7- DHC exists(173). Melanin is therefore an important variable in the cutaneous production of vitamin D.

4.11 Ageing of the skin and skin thickness

Ageing changes the skin's structure. Skin thickness declines with age linearly after age 20(137). The vital previtamin D precursor, 7-HDC, also decreases as people age, reducing the capacity of the skin to photolysise Vitamin D_3. In one study when young subjects are exposed to 15 minutes of solar radiation (apparently the equivalent of being in Cape Cod on a sunny afternoon), serum concentrations of Vitamin D reach 78.1nmol/l within 24 hours, yet older subjects were only able to reach a quarter of this concentration (20.8 nmol/l)(139). Elderly people often become Vitamin D deficient, the consequences of which are vital for bone health. Older people also may spend more time indoors and in some cases, be institutionalised.

4.12 Season and time of day

Both season and time of day affect the angle of the zenith of the sun, which in turn determines how much solar radiation reaches the earth. During the winter months the angle of the zenith is increased which results in greater concentration of ozone blocking the path of solar radiation. The mechanism of Raleigh scattering by air molecules is more pronounced where the path length is long. The process is inversely related to the fourth power of the wavelength, therefore, UVB and UVC being short wavelengths are strongly scattered by this process(138). Levels of terrestrial UVB will also be affected by the reflectance of the surface, as back scattering can occur(138).

Figure 13: Solar Zenith angle

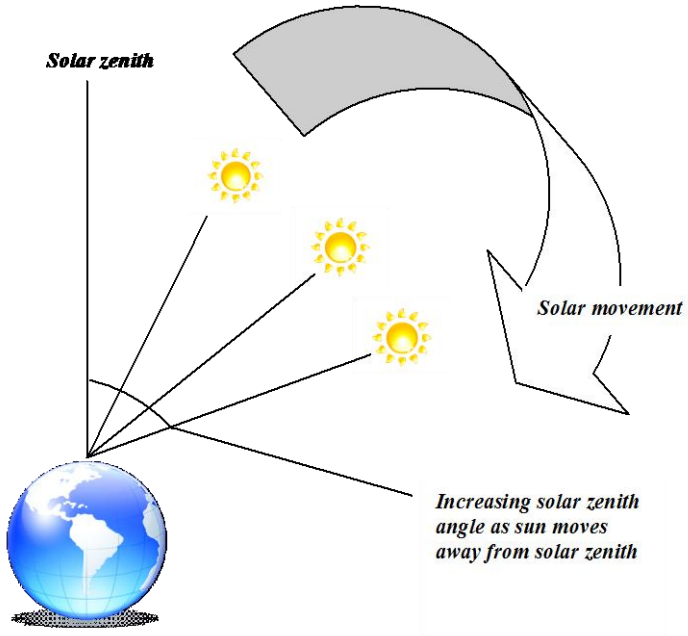


Figure 13 demonstrates that the zenith angle varies considerably from latitude to latitude. The angle observed at the equator is perpendicular but increasing zenith angles are observed with increasing latitude. Increasing latitude is therefore associated with decreasing UV intensity as the volume of ozone penetration increases, filtering out high energy photons. This markedly affects the potential for Vitamin D

production in human skin and, thus, the seasonal flux of population levels of Vitamin D during different seasons.

4.13 Sunscreen

Concern about exposure to high energy UVR and the increasing incidence of cutaneous cancers has led to the promotion of sunscreens to the general public. Whilst sunscreens can be very effective in protecting the skin from the damaging effects of the sun, they may also inhibit the cutaneous production of Vitamin D_3 as they filter out high energy UVR(174). Use of sun factor protection 8 is enough to inhibit this process. This has been shown to be important in elderly subjects who, as a result of the natural decline in capacity to produce Vitamin D cutaneously, will demonstrate even less ability to do so with the persistent use of sunscreens(175).

4.14 Seasonal fluctuation

Given the effect of season, determined by the earth's position to the sun, there are marked variations in Vitamin D concentrations throughout the year, in any given population, in Europe. Limited UVB in the winter months causes Vitamin D concentrations to decline in the absence of supplementation or a specifically Vitamin D focused diet . It has been reported that the presence of UVB between October and April at latitude of 52 North is negligible (based upon modelled data). London latitude is 51 degrees north. Closer to the equator, where seasonal variation is less dramatic, it is possible to synthesise Vitamin D cutaneously all year round. No studies that specifically examined the UV exposure of Londoners were identified.

4.15 The problem

The question remains, is vitamin D deficiency in Tuberculosis patients caused by lack of sunlight? It has been reported that those with Tuberculosis do appear to have lower levels of Vitamin D than healthy controls(147;156;176). Yet the direction of the relationship remains unclear. I.e., do low levels of Vitamin D, caused by lack of sunlight lead to the reactivation of disease or does active disease cause the Vitamin D deficiency?

Only one group of researchers has attempted to directly answer this question; Lumsden et al(177). They studied 178 London patients with culture positive Tuberculosis and 130 healthy ethnically matched controls and compared their vitamin D levels at presentation and through- out a one year period. They measured skin colour using a colour scale, whereby an assessment of skin colour was made by eye as corresponding to either 'dark', 'mid' 'brown' and 'light' i.e. white skin. A sub-set of the total sample was also assessed for dietary intake, although not all. Dietary intake was assessed in 35 patients and 35 controls that completed a food frequency questionnaire. Measures of sunlight exposure were assessed using a questionnaire which included assessments of season, latitude, time of day and weather conditions and sunscreen use. They state in their paper, that as *'London's latitude is 52 degrees north, there is 'no radiation of the appropriate wavelength (290-310nm) from the end of October to the end of March'(177).*This assumption was based upon a study by Webb et al that modelled predicted levels of Vitamin D synthesis using bottled 7-HDC(169). Webb's group concluded from this study that in order to maintain year long adequate Vitamin D levels, a person would need to spend 1-2 hours daily in summer sunlight, exposing the hands, face and legs(169). This assumption was used as the basis of the estimate of adequate sun exposure by the Lumsden group, along with the other factors described. They found that the mean levels of vitamin D were significantly lower statistically in the TB group when compared with controls and this supported the work of others(6;142;147;148;156;176). They also found that skin colour was not a significant factor in vitamin D deficiency in the TB or the control group and this contradicted the work of others(173). An increase in Vitamin D status was observed in healthy controls following summer months but this effect was absent in the TB group. Why was this? The Lumsden group report that the difference in Vitamin D levels between TB patients and controls was unrelated to skin colour, sun exposure and diet, even though the presence of these factors were comparable across the groups. They conclude that other factors may be present that influence Vitamin D deficiency in those with Tuberculosis.

One of the problems drawn from their conclusions, which they readily acknowledge, is that both measures of skin colour and sunlight exposure were inadequate. Visual rating of skin colour is open to error(178) and so too can sun exposure questionnaires result in imprecise estimates on sunlight exposure(153). There is a further problem in

that estimates of sunlight exposure were made from data 'modelled' from sunlight studies in Boston, USA and these studies were not conducted using live ambient subjects. It may be that the external validity of the Boston work is questionable given the potential variations in conditions between different cities as well as the potential for data to vary according to the method chosen to estimate the ability of human skin to generate Vitamin D. In order to build upon the foundations laid down by Lumsden, it would be necessary to identify a suitable and acceptable method of measuring sunlight exposure in a Tuberculosis group to provide a more precise measure than a questionnaire. Additionally, an objective method of measuring skin colour and the relationship between skin colour, sunlight exposure and Vitamin D synthesis would be beneficial in understanding the significance of sunlight exposure to Vitamin D status in a Tuberculosis group.

4.16 Hypothesis

Given what is known about the relationship between active Tuberculosis and Vitamin D deficiency and the stated uncertainly regarding the role of sunlight exposure in the resulting Vitamin D deficiency, I wished to test the following null hypothesis:

Sunlight exposure is not significantly associated with Vitamin D deficiency in Tuberculosis patients.

In order to test this null hypothesis, and measure the contribution of the main variable of interest, it was necessary to answer other questions regarding the known variables that may influence Vitamin D status in order to obtain a full understanding of the contribution of each. I proposed the following research questions:

1. What is the contribution of sunlight to Vitamin D status in TB patients and unaffected controls?
2. Is Vitamin D deficiency in active patients and contacts explained by differences in sun exposure and other factors that influence Vitamin D status?
3. What are the differences in dietary intake of Vitamin D between index cases and unaffected contacts and how does this relate to Vitamin D status?
4. Does being in the city affect potential UVR exposures?

5 Chapter 5: Method development

I began by investigating how one would measure the variables of interest more accurately than has been previously attempted in a Tuberculosis sample. This chapter reports my rationale for the method selection in order to measure the variables of interest. First of all, it was necessary to deploy methods to measure:

- UVB Exposure
- Skin type
- Vitamin D status
- TB status
- Skin exposure

The following reports the methods selected, the rationale for their employment, and the results of pilot experiments are reported in the next chapter.

5.1 Personal Dosimetry: Measuring UVB exposure

UVR can be measured in W/m² and weighted for varying biological effects for different 'action spectrums'(171). There is a wavelength dependence of action spectra of the different UV induced photo-biological effects(179). Personal dosimetry for research purposes should reflect the appropriate spectral response being measured. Action spectra are defined in terms of their effects on biological systems; the most commonly used are the CIE erythermal action spectrum(180) and the CIE photo carcinogenesis action spectrum(171). Action spectra have also been estimated for ocular effects and tanning. Predominantly, the most effective wavelength biologically, lies in the bandwidth UVB (290-320 nm). The erythemal action spectra is very close to the Vitamin D action spectra. Although not identical, their agreement is such that most frequently in sun exposure studies the erythemal action spectra is used in place of the Vitamin D action spectra.

In order to begin, a simple, acceptable and precise method was required to measure sunlight exposure in subjects in the field study. More precisely, a method was required that would allow measurement of personal ambient UVB exposure. i.e. *'the fraction of the total available UVR that a person gets relative to a horizontal*

plane'(171). This exposure fraction can be calculated into a personal UV dose. These doses are commonly expressed as MED (minimal erythemal dose) and SED (standard erythemal dose), which are a measure of personal radiant exposure, expressed in J/m²(181).

Polysulphone film badges have been used successfully in a number of populations and age groups for this purpose(182;182-186). The films have been used for a number of years and were first proposed as a possible UV dosimeter by Davis et al in 1976(179). Other studies have since reported the use of polysulphone films in sun exposure studies in a wide variety of populations and settings, including children, young people and sportsman, in occupational as well as leisure contexts(187-190). The badges can be easily attached to the lapel of external clothing whilst outdoors and are inexpensive(179). They can also be used for the measurement of total available outdoor irradiance(171) as we shall see later on in this thesis. Polysulphone films are stable at extreme temperatures and can even be used under water (191). Other types of films do exist. For example, bio-films that employ the *Bacillus subtilis* spore, can be calibrated to mirror the erythemal response of human skin(185). These too have shown to be effective dosimeters. However, one disadvantage of this type of film is the requirement for differently calibrated films according to skin types. Once the Polysulphone films are exposed to ultraviolet radiation in the waveband 290-315 nm, the optical absorbance increases in a dose dependent manner(179). The change in absorbance can be determined by reading the film prior to and after exposure in a spectrophotometer. The SED or MED can then be calculated using a simple equation.

5.2 Minimal Erythemal Dose (SED) verses Standard Erythemal Dose (MED) as an expression of personal UVR exposure

Much research involving UV dosimetry has taken the (MED) as an expression of personal UV exposure. The MED is defined as the minimum amount of biologically weighted UV that causes a just perceptible redness in previously un-acclimatised white skin at 24 hours. The point at which this perceptible redness occurs, however, depends upon the skin type of the individual being exposed, thus it is not a very precise measurement. The SED is therefore the preferred measure(181) and is equal to a single dose of 100 J/m² and does not differ according to skin type. Additional to the requirement of dose measurement, one also needs to consider the time a subject is

exposed to the energy source and the quantity of skin exposed. It is for this reason that sun exposure diaries should be used in conjunction with the films to provide this data.

5.3 Determination of Skin type

The characteristics of skin that potentially affect Vitamin D synthesis needed to be quantified in order to determine their contribution to Vitamin D status in the field study. The Photo-reactivity of the skin describes its response when exposed to UVR. Classically, this quality of skin has been classified using four-six groups, defined by Fitzpatrick et al(192), and these have been widely used in clinical practice and research studies. Recently, a simpler version has been described by Diffey et al(193). These workers use only three categories to describe photo-reactivity rather than phenotype and burning potential and they classify skin type according to its ability to tan. Prior to starting this study this new scale had not been previously reported in the literature but, recently, it has been claimed that the Diffey scale is more sensitive in identifying sunburn sensitivity that more closely reflects the erythemal response than Fitzpatrick(193). Scales for measuring photo reactive skin type are widely used in clinical research, yet they do not always reflect a subject's ability to accurately report reactions of their skin to the sun. This is partly because long-term memory recall is not always accurate(194). For this reason both scales were employed in this study alongside an objective measurement of melanin, which is described in the next section. Both scales can be viewed in Table 19 and Table 20.

Table 19: Diffey - Skin photo-sensitivity classifications

Trigger question: If you are going out in strong summer sunshine, which answer best describes how you might react?

Category	Response
1	I take care not to expose my skin too long without any protection as I have the sort of skin that burns very easily and, if I'm not careful, the redness can last for several days or more and my skin may peel
2	I don't worry too much about protecting my skin unless I intend staying out for an hour or more as I have the sort of skin that seems to tolerate the sun well, especially after a few days of sun exposure.
3	Sun exposure is not a problem for me as I was born with dark skin and cannot remember getting red, burnt skin from staying in the sun too long.

Table 20: Fitzpatrick –Skin photosensitivity classifications

Category	Response
1	I have extremely fair skin. I always burn and never tan
2	I have fair skin. I always burn and sometimes tan
3	I have pale coloured skin. Sometimes burn but always tan
4	I have an olive skin. I rarely burn and always tan
5	I have a moderately pigmented brown skin which never burns and always tans
6	I have markedly pigmented black skin which never burns and always tans

5.4 Methods and instruments for measuring melanin

5.4.1 Rationale

Being able to classify the skin's behaviour easily using a self-reported scale is one way of describing how melanin might influence the synthesis of Vitamin D in varying skin colours, as it is melanin that determines the skin's photo-reactivity. Therefore, since melanin is such an important variable and a degree of unreliability has been previously reported, an objective method of measurement was sought for use in the main study. The main experiment included subjects with Tuberculosis, as the disease occurs more frequently within minority populations; many patients suffering from TB also have darkly pigmented skin. It was important to determine how the quantity of melanin related to vitamin D status in these subjects and to select a reliable method of measuring it.

Colour estimation by eye, is a subjective activity and colour perception is influenced by many things: the intensity of the ambient light, eye adaptation to other colours seen before hand and the eye's ability to discriminate various shades of colour easily(178). Light reflectance technology on the other hand has been used in a number of research and clinical situations to accurately determine skin colour and melanin content specifically(178;195). The erythema meter produced by Dia-stron measures the amounts of the two main skin chromophores, haemoglobin and melanin, for which it has specific glass filters fitted. A tungsten-halogen lamp shines white light into a fibre optic probe. The light produced by this probe, when placed on the skin, will

scatter and reflect, depending on the chromophores present within the skin. The light omitted by the instrument is measured by three wavelengths.

546 nm (green)
632 nm (orange/red)
905 nm (near infrared)

In the case of measuring melanin pigment the 632nm filter is sensitive to the amount of melanin present in the skin and the 905nm filter is used as a reference signal.

The melanin index =
Log10 (905 nm/632 nm)*1000

For each measurement, the amount of scattering and reflection of light is analysed by the instrument and expressed as a melanin and erythemal 'index'. The main field

The complete range of the instrument = +999 to –999 melanin units. The main field study only considered the melanin index.

5.5 Measuring vitamin D status

Vitamin D is the general term used to describe Colecalciferol (Vitamin D_3) and Ergocalciferol (Vitamin D_2) serum concentrations. 25(OH)D is the sum of both Vitamin D_2 and Vitamin D_3. Both these components of Vitamin D belong to the steroid family and therefore biologically resemble a hormone more than a 'true' nutrient, i.e. a substance that is ingested from diet alone. Vitamin D_3 is produced in the skin in response to sunlight or ingestion of oily fish and fish liver oils and fish synthesise Vitamin D in the same manner that humans do. Vitamin D_2 is synthesised in fungal cells following irradiation from UVR(196;197). Vitamin D from either of these sources is metabolised by the liver to 25(OH)D and, it is this metabolite that is used principally to determine Vitamin D status(197). 25(OH)D is further metabolised by an enzyme 25(OH)D-1α-hydroxylase to 1, 25$(OH)_2D_3$, the active biological form of Vitamin D. Various cells and tissues in the body have the ability to hydoxylate 25(OH)D via this enzyme, giving rise to the biological actions of this metabolite. Expression of 1, 25$(OH)_2D_3$ is very tightly regulated by the endocrine system, and levels fluctuate according to endocrine activity. It is not, therefore, a very reliable

measure of ingested Vitamin D or that generated by sunlight. In the field study Vitamin D status was determined by measuring 25(OH) D using LC-MS/MS (Liquid Chromatography-tandem Mass Spectrometry) at Northwick Park Hospital, which participates in the international vitamin D external quality assessment programme.

5.6 TB status

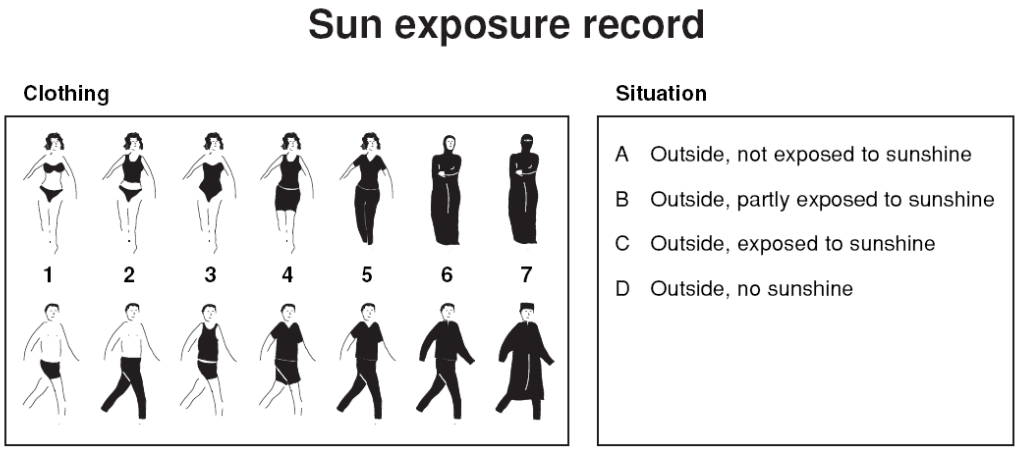
The literature provides reports where the authors claim that they have compared a variable of interest between patients with TB and those who have been infected but do not have disease. The methods used previously to exclude TB have not been sufficiently accurate to be sure of a person's TB status; infected or not. For instance, in the study by Lumsden et al (2005)(152), the researchers used Tuberculin skin test (TST) as a means to discriminate between those who were infected and those with latent disease. Up until recently, it has been impossible to tell who has been infected with TB, as there has been no definitive test that is able to detect latent disease. The TST skin test has been used for over a century and is commonly employed in clinical practice and research purposes, in the context of wider clinical information, to determine a person's TB status. The strength of the reaction in the skin following the subcutaneous or sub-dermal injection of Tuberculin provides an indication of the likelihood that a person has been infected with TB or has active disease. However, the results of such tests are confounded by the affect of the *Calmette-Guenin* vaccine (BCG) as is it derived from an organism closely related to the TB bacillus. The immune response to exposure of the skin test in individuals with recent BCG vaccine can mimic the positive reactions seen in infected individuals. The possibility of false-positive reactions as a result of vaccination has been shown to decline over time(198) but remains a significant problem for accurate diagnosis. False positive reactions to tuberculin skin tests have been described in relation to previous infection with non *TB mycobacterium*, which further complicates the diagnostic potential of the test(199). The problems of the skin test are confounded by the weak immune response of those who are immune-compromised. For this reason and due to the importance TB diagnosis presents in public health strategy, a new method was developed that relies on the T cell response to Mycobacterium specific antigens in the body (early secretary antigenic target (ESAT-6) and culture filtrate protein-10(CFP-10). Interferon Gamma release assay (IGRA) technology is now becoming more widely used in TB

diagnostics than at the start of this study. These tests have greater specificity in BCG vaccinated subjects and are less biased by environmental *mycobacterium,* unlike the skin test(200). During the pilot phase, I tested the feasibility of one such test, due to the reported superiority of its diagnostic potential(200). The ELISPOT (T-spot *TB*) produced by Oxford Immunotec, Oxford, UK, reports high sensitivity to the T cell response (96.6% compared with TST 66.7%(201). This test employs the use of peripheral blood mononuclear cells. My early experience of the ELISPOT showed that the test was complicated, required significant laboratory skill, was time consuming and relied upon the operator being available at certain times to conduct aspects of the assay. I concluded that with the resources available, in terms of time, funding and quality control, it was more realistic to employ a whole blood assay, undertaken at a laboratory that had experience in the method and was able to determine a high quality result. QuantiFERON-TB was used as an alternative. This test also uses the T cell response to the specified antigens but is a whole blood test and requires less complicated handling. Reports show superior specificity over TST: 91.6 versus 84.7 and a higher specificity over the ELISPOT test (91.6 versus 84.7). ELISPOT shows greater sensitivity compared with QuantiFERON (83-95%) compared with 73-83% for QuantiFERON(202;203). It was important to ensure the precision of TB diagnosis for the subjects, in case a healthy contact was identified as having latent TB unexpectedly and would therefore not fit the inclusion criteria of the healthy contact group.

5.7 Skin exposure-sun exposure diary

As previously noted, a simple sun exposure diary should be used in conjunction with the Polysulphone film badges in order to estimate the effect of the other factors that are known to be significant in a person's ability to synthesis Vitamin D. The most important of these is the proportion of skin exposed when outdoors, as when used in conjunction with the Polysulphone film, it will allow an estimation of the dose of sunlight received(204-206). A simple pictorial key was provided by Dr Alastair McKinley of the radiological Protection Board and I adapted this to reflect the type of dress that the target groups might be familiar with. Given that there was a significant Muslim component to the target population, I included specific dress styles that were relevant to that community. Figure 14 shows the dress key:

Figure 14: Skin exposure picture card



The above key shows the picture key that was used in the study and was later incorporated into the study questionnaire that also assessed dietary intake, sunscreen use other factors. The clothing key is designed to represent possible scenarios of dress across seasons and situations. Figure 1, 2, 3 and 4 depict situations that might occur during summer months or warm days during beach and recreational activity, whilst figures 5, 6 and 7 reflect likely dress scenarios for autumn and winter days. The estimation of skin exposure using this key was reflected as exposure of hands and face= 6% body surface exposed+ short sleeved shirt=20%+ shorts and skirt=40% and swimsuit=80% of body exposed(204-206). Complete covering of the face with a veil, a practice adopted by some Muslim women would result in total coverage with no skin exposed.

5.8 Summary

Table 21 shows the final method selection for the study. The testing of these methods is now presented in the following chapter, prior to the main experiment with the Tuberculosis group.

Table 21: Methods selected

Variable	Method selected	Instrument
UVB exposure	Polysulphone film	Polysulphone film badge
Photo-reactive skin type	Fitzpatrick photo reactive skin type classification	1. Self-reported classification table
	Diffey photo reactive skin type classification	2. Self-reported classification table
Melanin	Light reflectance	Dia-strom erthema metre
Vitamin D status	Measurement of serum 25 (OH)D	Liquid chromatography-tandem mass spectrometry
TB status	T-cell response to Tuberculosis bacillus specific antigens	Interferon gamma release assay (ELISA)
Skin exposure	Pictorial representation of clothing and skin exposure	Questionnaire component (sun exposure records)

6 Chapter 6: Pilot experiments

In the previous chapter I have described the method selected and the variables of interest they will be employed to measure. This chapter reports the results of a series of pilot experiments designed to ensure the chosen methods were reliable and also that I was familiar enough with the methods to prevent measurement error due to unfamiliarity with the instruments and or methods.

6.1 Pilot Experiment of films

It was important to pilot the use of the films for two reasons. One was that there were no reports in the literature relating to their acceptability, in terms of ease of use from the point of view of the participants who had taken part in various sun exposure studies, regardless of the fact that they have been used in a number of populations including children(187-191). Also, there was no discussion in the literature regarding any problems that might occur with the films and these were important to determine. If any problems did occur these could be rectified prior to the main experiment.

6.1.1 Description of film properties

Small squares of 40µm thick Polysulphone film (6x6) were mounted in cardboard frames and were prepared and provided by Dr Ann Webb's laboratory in Manchester, UK.

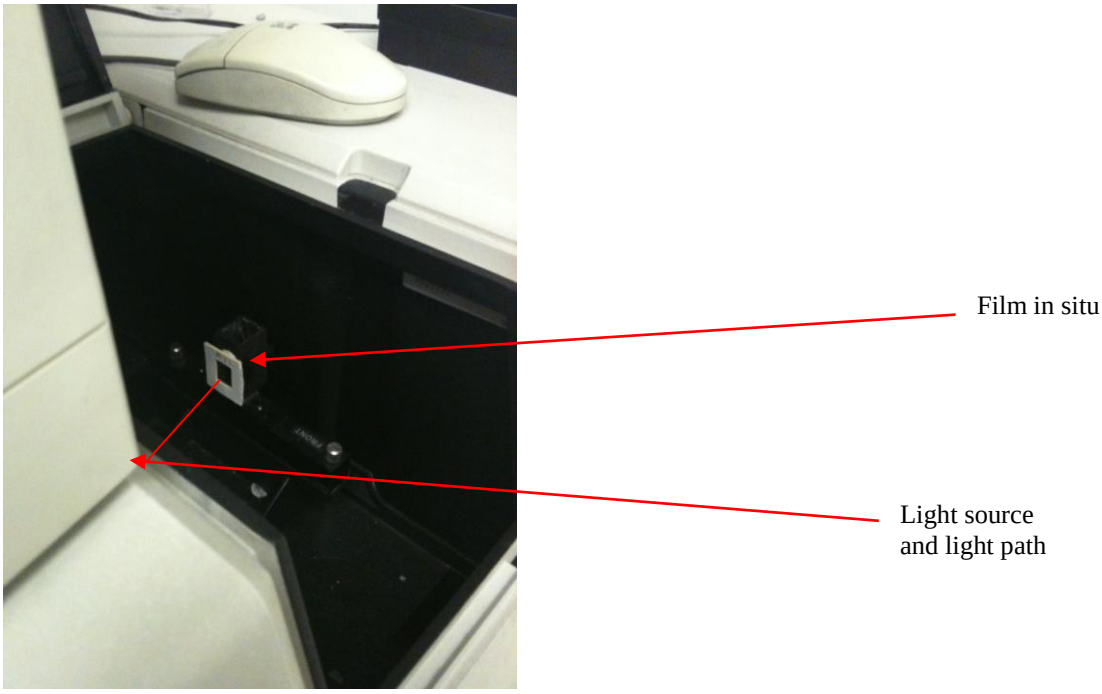
6.1.2 Reliability of films

6.1.2.1 Rationale

Before the films could be piloted, it was important to determine whether the point of measurement across the surface of the film was significant in terms of the possible variation in measurement that could occur. In order to read the films, each one had to be attached with adhesive to a metal frame within the spectrophotometer, as there was no sleeve within the machine itself that was able to hold the cardboard mount of the film in the same position each time (Figure 15). The lack of a film holder resulted in each film being placed slightly differently in the machine each time the film was read. As it was possible that this slight difference in positioning would alter the point that the beam passed through the film during measurement, it was important to check that following exposure, the change in absorbance was uniform across the film, to

minimise any errors in measurement. Therefore, an experiment was designed that would test this.

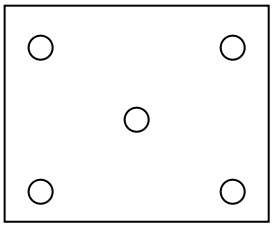
Figure 15: Placement of film in the Spectrophotometer



6.1.3 Method

Five unexposed films were placed in a Beckman DU 650 spectrophotometer, as above, and read at five different points of the film at 330 nm. Figure 16 shows approximately where the beam was passed through each film. The co-efficient of variance in the readings of the films was then calculated.

Figure 16: Approximate location of beam through PS films



6.1.4 Results

Table 22: Co-efficient of variation in film measurements

Film number	Mean	Standard Deviation	Co-efficient of variance (%)
1	**.2091**	.0118	**5.6**
2	**.2441**	.0819	**33**
3	**.2112**	.0071	**3.3**
4	**.1965**	.0032	**1.6**
5	**.2056**	.0201	**9.7**
Mean variation			**10.64**

Table 22 shows that the coefficient of variation of the measurements across the films ranged from 1.6% to 33%. Four films had a coefficient between 1 and 5% with only one film showing quite high variance (33%).

6.1.5 Discussion

The surprising variance of 33% in one of the films demonstrates the potential for rogue films, although method errors may have occurred because of unfamiliarity of technique and the equipment being used. The films appeared to be stable regardless of their position in the machine with the exception of the one outlier. The mean variance of the five films was 10.64%. A larger sample of films may have shown a reduction in this figure. The rogue film in the small sample left me a little concerned. During the field study, I ran this experiment as a data quality check in a random sample of 10% of the film batch. This small experiment was conducted pre- exposure of the film.

6.2 Experiment 2: Exposure of film and degradation of polymer

6.2.1 Rationale

The films are reported to degrade in a dose dependent manner in the literature(179). In order to check this characteristic it was necessary to test them under controlled laboratory conditions where the dose of UVR was determined by a controlled energy source.

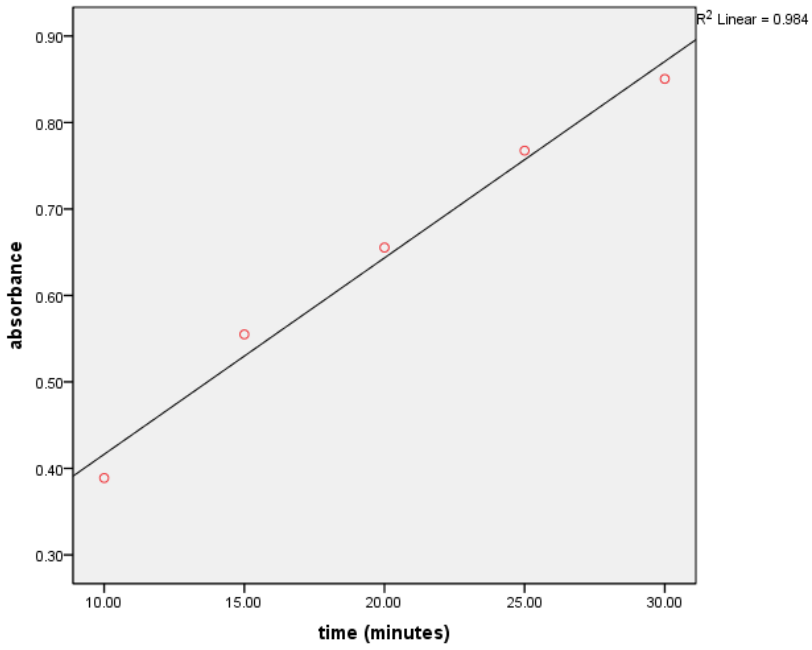
6.2.2 Method

An unexposed film was placed beneath a Fotodyre 3504 Tran illuminator short wave lamp, and was exposed for 10, 15, 20, 25 and 30 minutes and read in a spectrophotomer at 330 nm. These times were chosen to achieve a high degree of saturation of the film that would represent a typical summer's day sunshine in the UK, approximately 23 SEDS, taken from radiological board measurements(207) . At each increment of time the film was read and a measurement taken.

6.2.3 Results

Figure 17 shows a scatter plot that illustrates the correlation between absorbance of the film and time spent beneath the short wave lamp. The x axis shows the time of exposure in minutes, ranging from 10 to 30 and the y axis shows absorbance values.

Figure 17: Absorbance of Polysulphone film and time exposed



6.2.4 Discussion

Figure 17 demonstrates the visual correlation of exposure and degradation within the polymer in a dose -dependent manner, as described in the literature. This characteristic is reflected in the increased absorbance potential of the film that demonstrates a linear relationship between the two variables tested. Other workers have reported increased variation at higher saturation levels, indicating that there is more risk of error at the higher end of the films' potential. I was reassured to see that the relationship between exposure and saturation remained linear up until about 0.8/0.9, suggesting a reliable and stable method of UV measurement.

6.3 Experiment 3: Were the films acceptable as a method of UV measurement in healthy controls?

6.3.1 Rationale

After I had tested the known sources of error associated with the use of the films it was important to also test how easily they could be used in a small sample of subjects prior to the field experiment. There were no reports of practical or acceptability problems with the films in the literature. As I has not used the method before I felt it was important to have an understanding of potential practical restraints of the method. The films were used in conjunction with a skin exposure diary, as described earlier, that included a pictorial representation of clothing styles and daily time spent outdoors. The type and amount of clothing worn has been shown to either hinder or facilitate UVR reaching the skin(175;208;209). It was therefore important to determine how easily the diaries could be used in conjunction with the films and how easily subjects could identify the visual picture keys on the diary card. The key was later incorporated into the questionnaire used in the main study.

6.3.2 Methods

Four healthy subjects were asked to wear the films for one week and complete the sun exposure diary whenever they were exposed to sunlight or daylight (Appendix 7). They were asked to secure the films to the lapel of their outside clothing with a safety pin as shown in Figure 18. The pilot took place during April and May in London 2009. The diary asked the participants to identify the times they were outside and for

how long. They were also asked to describe the extent of body exposure by referring to the clothing key on the diary. The situation of their exposure was also recorded and they were asked to identify whether they were outside exposed to sunshine, partly exposed, exposed or outside but not exposed to sunshine. They were also asked to report any 'problems' experienced wearing the films and whether they had any suggestions for easier use.

Figure 18: Subject wearing the Polysulphone film

Reproduced with permission from subject. Fitzpatrick Skin type 3

6.3.3 Results

Table 23 shows time spent outside over the monitoring period, skin type of the participant using the Fitzpatrick scale and the SED reflecting the total exposure over the 7 day period. Data ranged from 35 minutes to 3 hours and 15 minutes.

Table 23: Time outdoors (hrs and mins), skin type and SED in pilot group

Subject	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Total	Skin Type	SED
1	1.50	1.15	2.55	0.40	2.0	3.15	1.0	12.9	2	3.8
2	0.57	1.0	0.35	0.45	1.0	1.20	1.0	7.5	1	1.1
3	1.50	1.40	1.45	2.12	2.20	2.14	1.30	13.5	3	3.9
4	1.15	1.42	0.35	0.55	0.35	0.37	0.45	6.4	1	2.4

All subjects found the diaries easy to use and some comments were taken into account to clarify the instructions on the diary cards. Some subjects found the instructions relating to the exposure situation confusing, I.e. clarifying differences between 'outside and not exposed' and 'outside and partly exposed'. The subjects were exposed to varying levels of UVR between 07.00 and 21.30.

Table 24 describes the raw data for the pre and post exposure absorbance of the films and the calculated SED. The SED is a Quartic equation and is a function of the change in the film and is determined by multiplying the linear cubic equation by delta (post exposure – pre exposure / 1000). The SED ranged from 1.1 to 3.9 over the monitoring period. Figure 19 shows a box plot that illustrates the smallest observation (in hours), the lower quartile of the data, the median, the upper quartile and the largest observation and any unusual or extreme measurements. The plot shows that subject two had the lowest median sun exposure over the seven day period and shows some extreme values on day three and day six, when unusually low and high exposure times were noted. Subject three spent most time outdoors, with longer exposure times than the rest of the sample, whereas subject one showed the greatest range of exposure times over the seven day period.

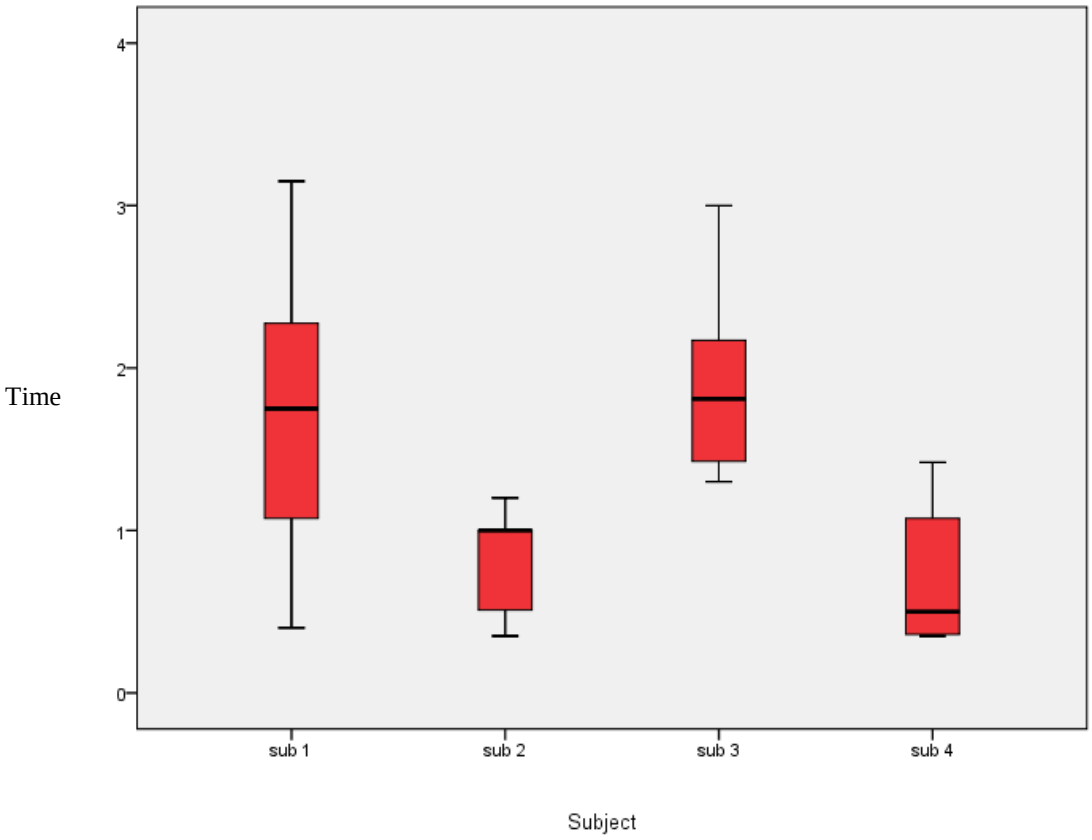
Table 24: SED in pilot group

Badge no.	Absorbance at 330nm		delta A (change in absorbance)	SED
	pre-exp	post-exp		
1	206	469	0.263	3.8
2	206	302	0.096	1.1
3	206	476	0.27	3.9
4	195	379	0.184	2.4

$$SED = 10.7(\Delta A330) + 14.3(\Delta A330)^2 - 26.4(\Delta A330)^3 + 89.1(\Delta A330)^4$$

Those that spent longer outdoors showed the greatest change in the absorbance of their films, with those spending least time outdoors revealing the smallest change. Subject 1 and 3 spent comparable time outdoors and this agreed with the exposure values of their films. Although the exposure time was similar, subject 2 reported only partial sun exposure during the monitoring period whereas subject 1 was exposed to clear sunshine on most days of exposure. Subject 1 also spent longer outdoors during the times of day when UVB is most prevalent, i.e. between 10.00 am and 15.00.

Figure 19: Time of exposure in hours per subject over a seven-day period



6.4 SED against weekly exposure times.

A Pearson's correlation was computed to assess the relationship between SED and weekly exposure times. There was a marked correlation between time outdoors and SED (r= .949 significant at .05). Values of 0 indicate no relationship between the variables whilst values of 1 show a perfect relationship. It is acknowledged that the data points are very limited in this experiment even though the direction of the relationship was as expected.

6.5 Discussion and conclusion

The film exposure and reported SED correlated well with the time spent outdoors and the reported conditions of exposure. To determine the significance of the time exposed to sunshine one would need to also measure 25(OH)D, the internationally accepted standard of Vitamin D status. Those subjects who reported abundant sun exposure showed greater changes in the film absorbance, which corresponds well to

the behaviour of the films under controlled conditions. It is important to note that the SED measured by the film will only be a partial measure of the actual dose received by subjects. This factor will depend on clothing and therefore the percentage of bare skin exposed to sunlight. Inaccuracies in reporting any aspect of the monitoring situation could lead to error once these data are correlated to Vitamin D status. The diary card element of the measurement is therefore crucial in determining this element of UV dose calculation. In terms of ease of use of the film badges, no subject reported any particular problems wearing the films.

6.6 Skin type: how do the two scales compare?

6.6.1 Rationale

As I had decided to use both skin photo-type classification scales for the purpose of comparison alongside the objective measurement, it was necessary to see how the scales compared to each other in a small number of subjects with various skin tone and photosensitivity.

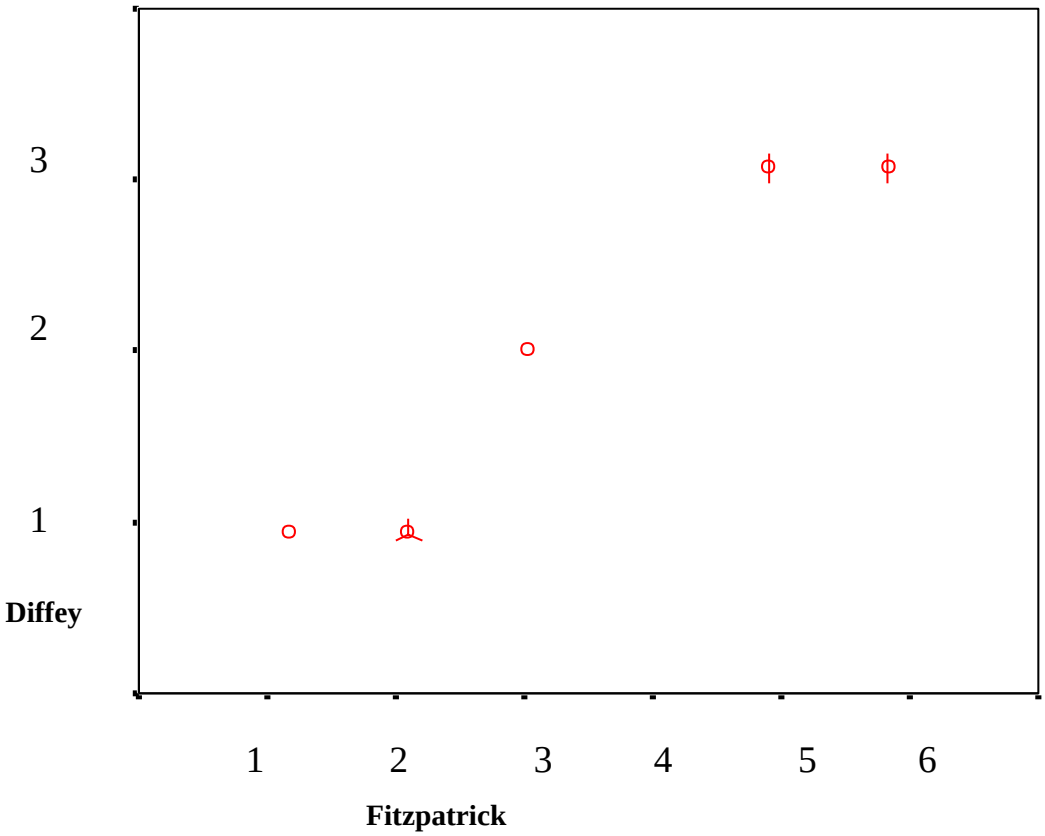
6.6.2 Methods

10 subjects of various skin colour were asked to complete a questionnaire (Appendix 7) and select the skin type described by both Fitzpatrick and Diffey that best described their skin‘s behaviour, after spending an hour in strong sunlight at midday.

6.6.3 Results

Figure 20 shows a scatter plot with ‘sun flowers’ to denote when more than one subject chose the same category. A single dot without a line denotes one subject, one with one horizontal line denotes two subjects, and one dot with three points denotes three subjects. The scatter plot shows that the scales correlated closely with each other. Lighter skinned individuals chose the lower categories and the darker skinned individuals chose the higher classifications of both scales. Table 25 shows a strong correlation between the two measuring scales with R= .937, n=9, P=0.01.

Figure 20: Relationship between Diffey and Fitzpatrick skin typing Matrix in pilot subjects. n=9



Single dot=1 subject, dot with vertical line =2, dot with 3 lines=4 subjects

Table 25: Correlations between Diffey and Fitzpatrick scales

			Diffey	Fitzpatrick
Spearman's rho	Diffey	Correlation Coefficient	1.000	.937**
		Sig. (2-tailed)	.	.000
		N	9	9
	Fitzpatrick	Correlation Coefficient	.937**	1.000
		Sig. (2-tailed)	.000	.
		N	9	9

**. Correlation is significant at the 0.01 level (2-tailed).

6.7 Testing the Erythema meter

6.7.1 Method

The instrument was placed on a hospital trolley and calibrated by placing the probe in the port and running the auto zero function. The meter is shown in Figure 21. Within the port a pure white light acts as a reference source. Ten 'healthy' subjects were asked to take part (one declined). Measurements were taken from two skin sites, one sun exposed site (the back of the hand) and one sun protected site (the inner upper aspect of the top of the arm). Measurements were obtained by placing the probe lightly against the subject's bare skin as illustrated in Figure 22. (The position of probe on the skin in the figure 18 is shown for illustrative purposes only). The machine was set in 'mean mode', where the instrument was able to calculate the mean measurement by taking 100 readings in quick succession. The upper inner aspect of the arm was used to provide a measure of the subject's constitutive melanin. That is, the genetically determined level of cutaneous melanin present in the skin that is shielded from the sun(210;211). The back of the hand, a frequent sun exposed site, reflected measurements of the subject's faculative pigmentation. The probe was placed flush against the skin using a black probe support, which both prevented extraneous light entering the measuring area altering the reading, and also supported the probe in an upright position to ensure consistent measurement. Three measurements were taken from each site, to ensure consistency of measurement. The results were also collated with the photosensitivity questionnaire, to describe the melanin content of each skin type.

Figure 21: Dia-stron Erythema Meter

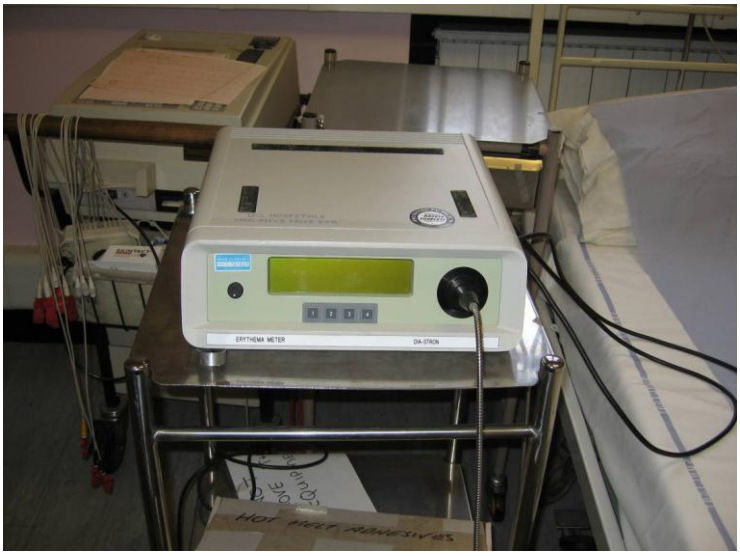
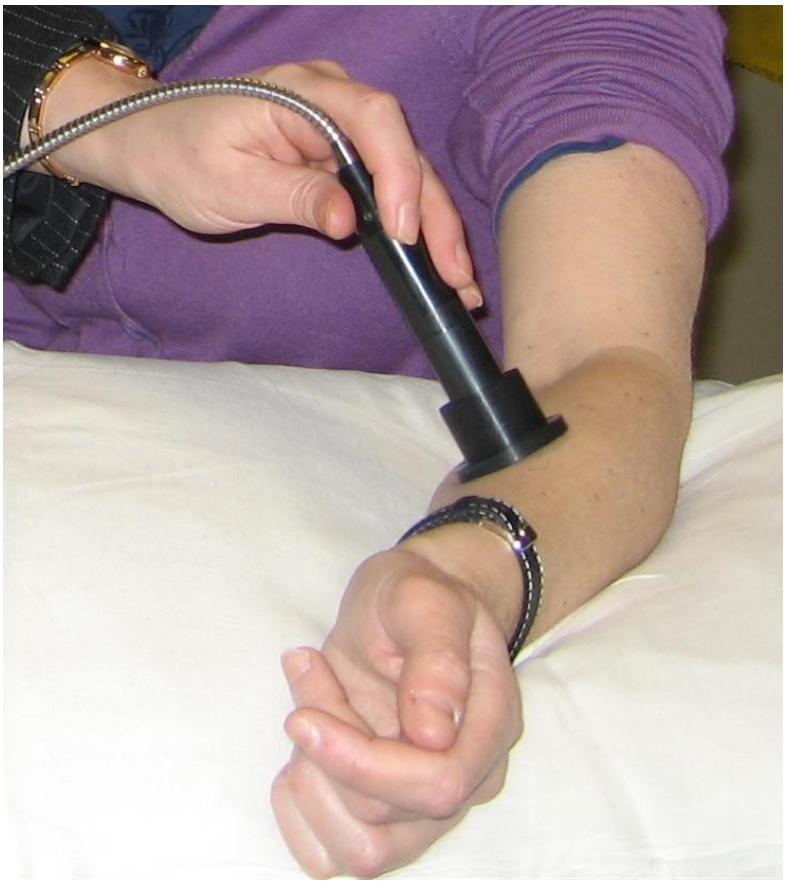


Figure 22: Measuring probe on subject's skin



Each measurement of melanin was taken three times in quick succession in all subjects and an independent operator also made the same measurements on each subject.

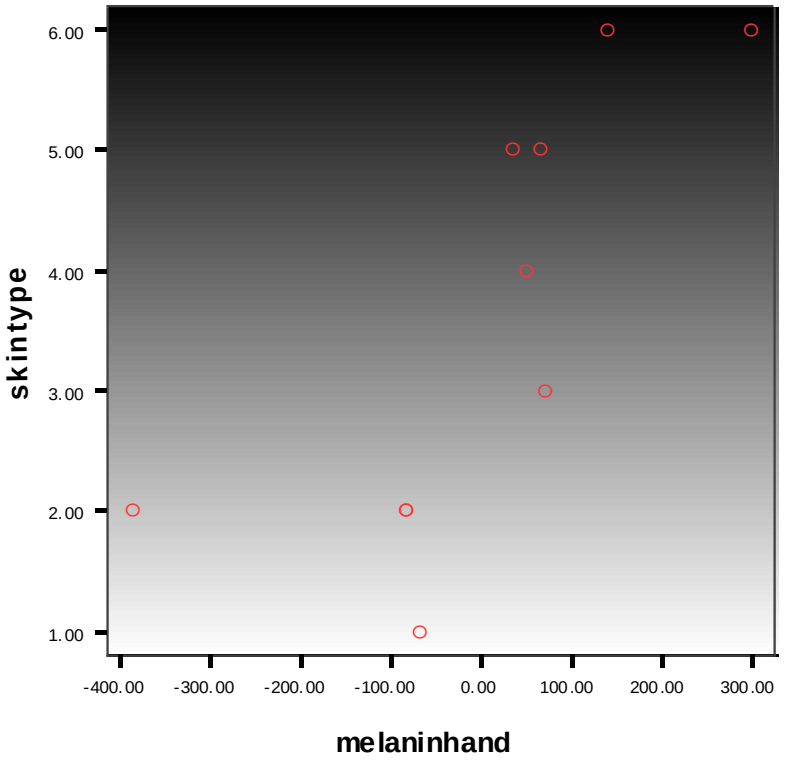
6.7.2 Results

Figure 23 shows a scatter plot that describes the relationship between skin category and melanin index using the Fitzpatrick categories. The plot shows that the melanin index increased in a linear fashion from very photosensitive skins to less photosensitive skins that do not burn.

The correlation co-efficient = Spearman's r= .815 (Table 26).

Values of 1 show perfect correlation.

Figure 23: Melanin index and reported skin type using the Fitzpatrick categories.



x-axis: melain index from the back of the hand as measured by Dia-stron erthyema metre. Range of instrument -999+999. A minus number indicates a paler skin (less melanin) whilst numbers greater than zero represent darker skins.

Table 26: Correlations melanin index and Fitzpatrick scale

			Melanin-hand	Skin-type Fitzpatrick
Spearman's rho	Melanin-hand	Correlation Coefficient	1.000	.815(**)
		Sig. (2-tailed)	.	.004
		N	9	9
	Skin-type Fitzpatrick	Correlation Coefficient	.815(**)	1.000
		Sig. (2-tailed)	.004	.
		N	9	9

** Correlation is significant at the 0.01 level (2-tailed).

When the subjects categorised their skin using the Diffey method (Figure 24), the relationship with the melanin index was also linear and strongly correlated the melanin index r= .817 (Table 27). The subjects who took part had a range of skin types from very fair skin to very black skin.

Figure 24: Melanin index and reported skin type using the Diffey categories (exposed site).

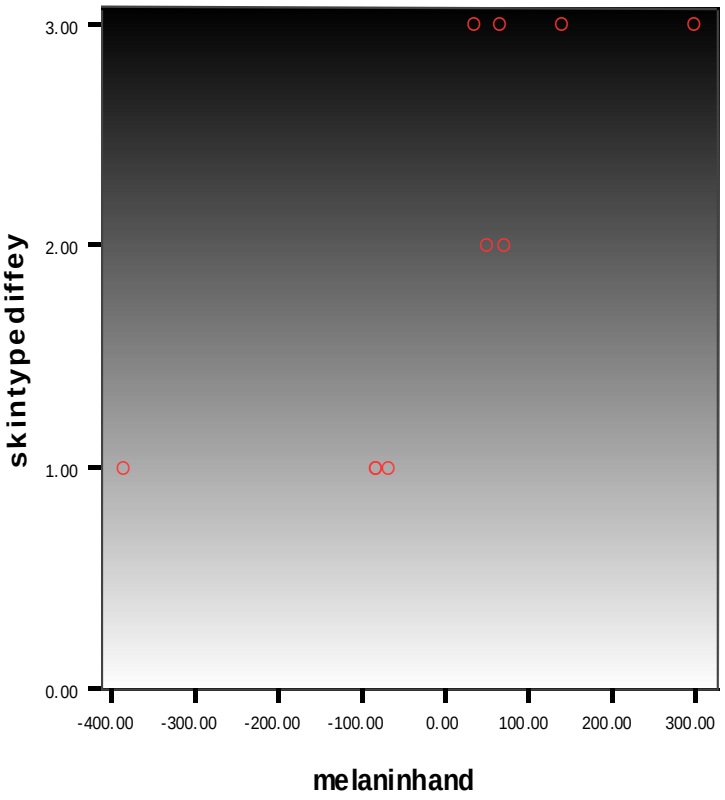


Table 27: Correlations between melanin index and Diffey scale

			Melanin-hand	Skin-type Diffey
Spearman's rho	Melanin-hand	Correlation Coefficient	1.000	.817(**)
		Sig. (2-tailed)	.	.004
		N	9	9
	Skin-type Diffey	Correlation Coefficient	.817(**)	1.000
		Sig. (2-tailed)	.004	.
		N	9	9

** Correlation is significant at the 0.01 level (2-tailed).

6.7.3 Conclusion

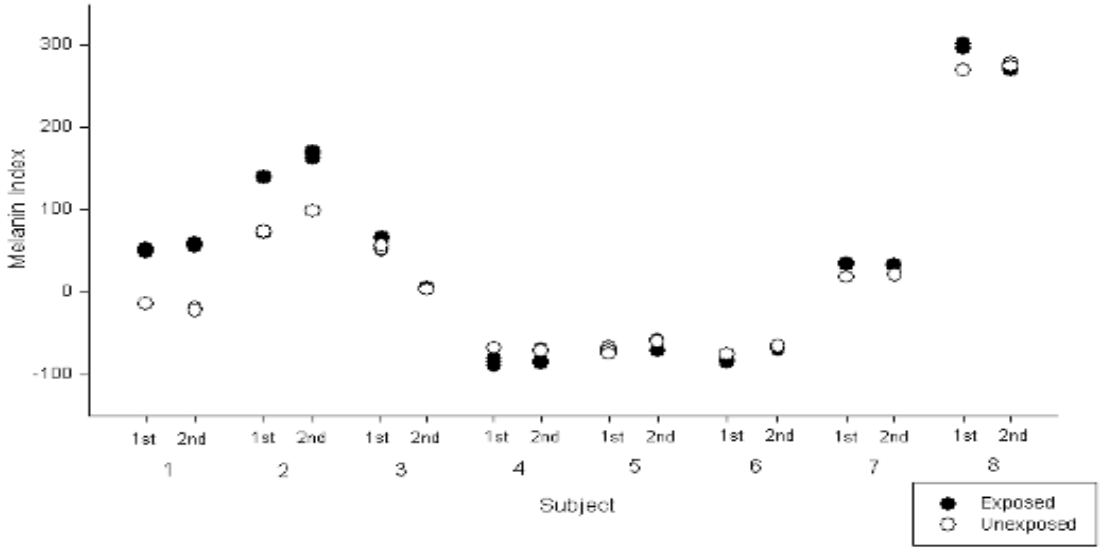
The melanin index correlated well with the self-reported photosensitivity using both the Diffey and Fitzpatrick scales. It was simple to use and acceptable for the subjects and provided an objective measure of skin melanin content.

6.8 The inter and intra-rater reliability of measurements

Figure 25 shows a graph that illustrates the measurements taken comparing two different operators. The x-axis shows the first and second operators' measurements and the y-axis shows the melanin index. The black dots denote the exposed skin site and the clear dots show the unexposed skin site where the measurements were taken. Measurements that are very close together appear as one single dot on the graph as seen in the first set of data.

The variance between measurements was no more than 10%. Each measurement taken reflected the mean of 100 measurements calculated by the machine in its 'mean mode', so the variance calculated between the three measurements equalled 300 measurements.

Figure 25: Inter and intra reliability of melanin measurements between raters and between subjects



6.8.1 Conclusion

I concluded that the erythemal meter was a simple and accurate method of measuring the melanin content of skin.

I was sufficiently reassured that the methods chosen in these pilot studies had stood the tests of experimentation and that potential errors that could occur in the main study had been significantly identified and reduced, to support or refute the questions which the next chapter of this thesis was to address. That is, the relationship between UV exposure and Vitamin D status in London TB population and the accurate measurement of the cofounding variables. The next section describes the main experiment using the selected methods. Some revisions were made to certain aspects of the study design and methodology as the study progressed. These amendments shall be explained with the rationale for their inclusion as they become relevant to the research report.

7 Chapter 7: Testing the contribution of sunlight exposure to Vitamin D deficiency in a TB population and contacts.

As a result of the testing of the instruments, I concluded that it was realistic to propose a powered study to answer the research questions. The methods had been thoroughly tested and the known potential sources of error were identified and rectified. Ethical approval for this study was obtained from Whittington and Moorfield's research ethics committee in July 2005 (Appendix 8).

7.1 Background and objectives

As described in chapter 4 the relationship between Vitamin D deficiency and active Tuberculosis has been described in numerous studies as being significantly lower than control subjects(143;212). Many researchers have explained this relationship by suggesting that lack of sunlight may be the cause. As none of the existing studies measured sunlight exposure directly in these subjects, the contribution of sunlight to Vitamin D deficiency in this group remains poorly understood. One study estimated sunlight exposure in a TB group using a questionnaire(152), however, as already discussed, no direct measurement of sunlight was employed in this group. As profound Vitamin D deficiency has also been noted in active Tuberculosis patients in sun rich climates, such as India, Africa and Australia(144-147), there remains the possibility that the disease process may be responsible in some way for the down regulation of Vitamin D at some point in its metabolism or equally, it is possible that low Vitamin D levels, as a result of lack of sunlight, influence reactivation of disease in infected individuals. The problem remains that the direction of this relationship has not been quantified. Therefore, a study was designed to test this relationship using a direct measure of sunlight exposure and other variables that may affect Vitamin D status as described and tested in the previous chapters.

7.2 Hypothesis

A study was designed to test the following null hypothesis:

Sunlight exposure is not significantly associated with Vitamin D deficiency in Tuberculosis patients.

7.3 Study design

A prospective comparative cohort design was selected to compare sunlight exposure and other variables that are known to affect Vitamin D status in Tuberculosis index cases and contact cases. Subjects were recruited in all seasons to reflect potential sunlight exposure throughout the typical UK seasonal year reflecting variations in sunlight distribution.

7.4 Inclusion/exclusion criteria

All index cases and their contacts who presented to a central London chest clinic were invited to take part. Inclusion criteria included a willingness to take part and the presence of active Tuberculosis disease defined by positive aurimine sputum smear, sputum culture or radiological evidence of significant clinical signs in the chest(104). Contacts were defined as those people who were also screened for TB as a result of close contact with an index case and also presented to clinic for such screening. All subjects were 18 years and over. Subjects with known serious liver disease, kidney disease and serious co-morbidities such as cancer were excluded as these factors are known to alter vitamin D metabolism(152). Those under the age of 18 and prisoners were also excluded.

7.5 Protocol refinement

I began with an attempt to match each index case with a control to ensure a contextual environmental comparison, I.e., by matching subjects, one could be more confident that the exposure conditions were similar to the index case. I attempted to recruit patients according to this schedule and according to the inclusion criteria stated above. I continued for four months, but failed to achieve any matched pairs. 33 index cases were screened and 12 contact cases. Of the index cases 7 refused; 2 were excluded as they had cancer; 1 was a prisoner; 1 lady was heavily pregnant and the nurses felt it would be too much strain for her to participate; 1 case was moving to Turkey, and 1 case had just flown in from Zambia and had been referred to the chest clinic by the airport. Even if this patient had agreed, he was not a London resident. Of the contact cases, 3 were reactive to IGRA but, unfortunately, either the matched index case refused or they did not know the index case. Of the 12 contact cases screened, I was unable to match them to an index case as either they were being treated elsewhere or

they refused to take part. At this point I acknowledged that unless the protocol was simplified it would not be possible achieve sufficient participation. With the approval of the ethics committee, I amended the protocol to compare unmatched groups of index and contact cases to allow greater opportunity for inclusion. I further simplified the study by eliminating the requirement of the daily sun exposure diary to render the 'work' required by patients less burdensome. To ensure that some estimation of UVR exposure to skin was included in the dataset, I included the sun exposure diary card in the questionnaire rather than the subjects having to complete the diary over the exposure period. The questionnaire included questions relating to dietary ingestion of Vitamin D and also asked about time spent outdoors. This allowed some calculation of exposure even if patients failed to return the films. The final study schematic can be seen in Figure 26.

Figure 26: Study schematic

Index cases	**Contact cases**
Information provided for study in clinic. Telephoned to obtain agreement to take part. Agreed to meet next clinic visit	Information provided for study in clinic. Telephoned to obtain agreement to take part. Agreed to meet next clinic visit
1st study visit –outcomes measured within first four weeks of antibiotic treatment: Consent obtained 1. Blood sample- IGRA 2. Blood sample- base line Vitamin D 3. Skin photo- reactivity assessed by subjects using Diffey and Fitzpatrick scale 4. Melanin index measured using dia-strom erythema metre 5. Time outdoors (winter summer, last two months) 6. Food frequency of Vitamin D rich foods recorded 7. 2 Polysulphone films provided and instruction given re use. 1st film to be used first four weeks. 2nd film to be used 2nd four weeks 8. Cosmetic use and sun-bed use 9. Recent travel to sun rich climate	**1st study visit –outcomes measured:** Consent obtained 1. Blood sample- IGRA 2. Blood sample- base line Vitamin D 3. Skin photo- reactivity assessed by subjects using Diffey and Fitzpatrick scale 4. Melanin index measured using dia-strom erythema metre 5. Time outdoors (winter summer, last two months) 6. Food frequency of Vitamin D rich foods recorded 7. 2 Polysulphone films provided and instruction given re use. 1st film to be used first four weeks. 2nd film to be used 2nd four weeks 8. Cosmetic use and sun bed use 9. Recent travel to sun-rich climate
 **Intervention** 8 weeks UVR monitoring	 **Intervention** 8 weeks UVR monitoring
2nd study visit All measurements repeated except IGRA	**2nd study visit** All measurements repeated except IGRA

7.6 The intervention

All patients presenting to the clinic with suspected active disease were invited to participate, as well as close contacts. Information leaflets were provided and the study explained by the investigator. The information leaflet and consent form can be viewed in Appendix 9. Contact cases included those who were family and friends who either lived with the index case, or had spent considerable time with them in an enclosed place (such as work or the home). During their next appointment I obtained consent after the participant and contacts had had time to consider whether they wished to take part. If they agreed, I took a blood sample to assess their baseline Vitamin D status and IGRA response. Index cases were recruited in the first four weeks of treatment in order to mitigate any treatment effect on Vitamin D status(212;213). New patients were informed about the study by the consultant or other medical staff treating them, or I approached the patients and contacts in the clinic after they had been seen by the consulting health professional. Skin types were classified as described in the pilot experiments, according to photo-type using Diffey and Fitzpatrick scales and melanin index was measured using light reflectance spectrometry. Melanin measurements were taken from the dorsum of the hand, the forehead, each cheek and the inner upper arm for measures of facultative melanin and constitutive melanin respectively. Additional questions were included about the frequency of Vitamin D rich foods, recent travel to sunny climates and other contributing factors such as sunscreen use, sunbathing and sun-bed use. If the subjects were unable to speak English, members of the family and friends were asked to act as translators. Close contacts were identified and approached in the same way.

7.7 Sun exposure assessment

After the base line data had been gathered at the first study visit, subjects were monitored for eight weeks and asked to wear a Polysulphone film when they were outdoors. The eight week time frame was chosen as the half-life of serum Vitamin D is reported to be approximately two months(214). Those who consented were given two films, one for the first four weeks of the study and the second film for the remaining four weeks. The purpose of this was twofold: changing the film half way through the study would ensure that the film did not saturate and would also ensure that it did not become too damaged, potentially affecting final measurements.

Subjects were asked to attach the film to the lapel of their outside clothing using a safety pin as described in the piloting of the films. They were also instructed not obscure the film with clothing or hair and to ensure that the window of the film was clearly exposed. Blood samples that were taken for baseline Vitamin D and IGRA were prepared as instructed by the manufacturer and stored in a -80ºC freezer, until such time as they could be analysed. Subjects were instructed to return eight weeks later, when the melanin measurements were repeated and the films returned. The films were read in a spectrophotometer as previously described.

7.8 Sample size

I began with the assumption that if it were possible to recruit enough subjects then the best case scenario would be to aim for a sample that has sufficient power to test the null hypothesis that there was no significant difference in Vitamin D status in the contact and index groups and then compare sunlight exposure between the groups. It would, therefore, be necessary to estimate the degree of difference prevalence that I could expect to see in serum Vitamin D status between these groups. In people with darker skins, particularly Asian populations, prevalence has been shown to range from 22% to 83% in some groups(215). Studies have shown that during the summer months in the UK, 38% of participants are vitamin D deficient in the above referenced study. During the winter this has been shown to increase to 85%(215). White controls have shown normal concentrations. Given the range of Vitamin D deficiency present, it would be reasonable and clinically important to be able to detect Vitamin D deficiency in this sample at 20%. With a minimum Odds ratio of 2.5 (two controls for each index case) it was planned to recruit 76 cases and 152 controls, giving 80% power at the 95% significance level. The sun exposure data from the index cases and controls would be compared for differences and this would be related to Vitamin D status and compared. Two controls per index case were initially included, as it was proposed that both uninfected and infected controls could be identified and compared for differences. However, as described earlier, the matched controls were dropped in favour of a simpler schematic therefore I aspired to recruit 76 cases in each group.

7.8.1 Recruitment of subjects

Recruitment for the study began in July 2009, continued for 18 months and finally stopped in January 2011. During that time I attended clinic most weeks, twice weekly. Once a week the consultant led a clinic where new cases were seen and treated and the second clinic saw the contact cases and was led by the TB specialist nurses.

7.8.2 Results

During the recruitment period, 47 index cases were invited to take part, but only 13 agreed to do so. 3, who initially agreed to take part, later changed their minds. Of the contact cases, 79 were invited and 22 agreed to take part; 5 were lost to follow up and 8 later changed their minds. Only 12 index cases and 13 contact cases completed the study(216).

Table 28 and Table 29 show the demographics and ethnicity of all patients screened, and Table 29 shows the overall characteristics of all the patients who were approached to take part and reflect a typical TB population, i.e. a high prevalence of Black African index cases and few White British cases. One can see that the White British cases are more predominant in the contact group.

Figure 27 details the demographic of both index and contact cases who completed the study.

Table 28: Demographics of all patients and contacts screened

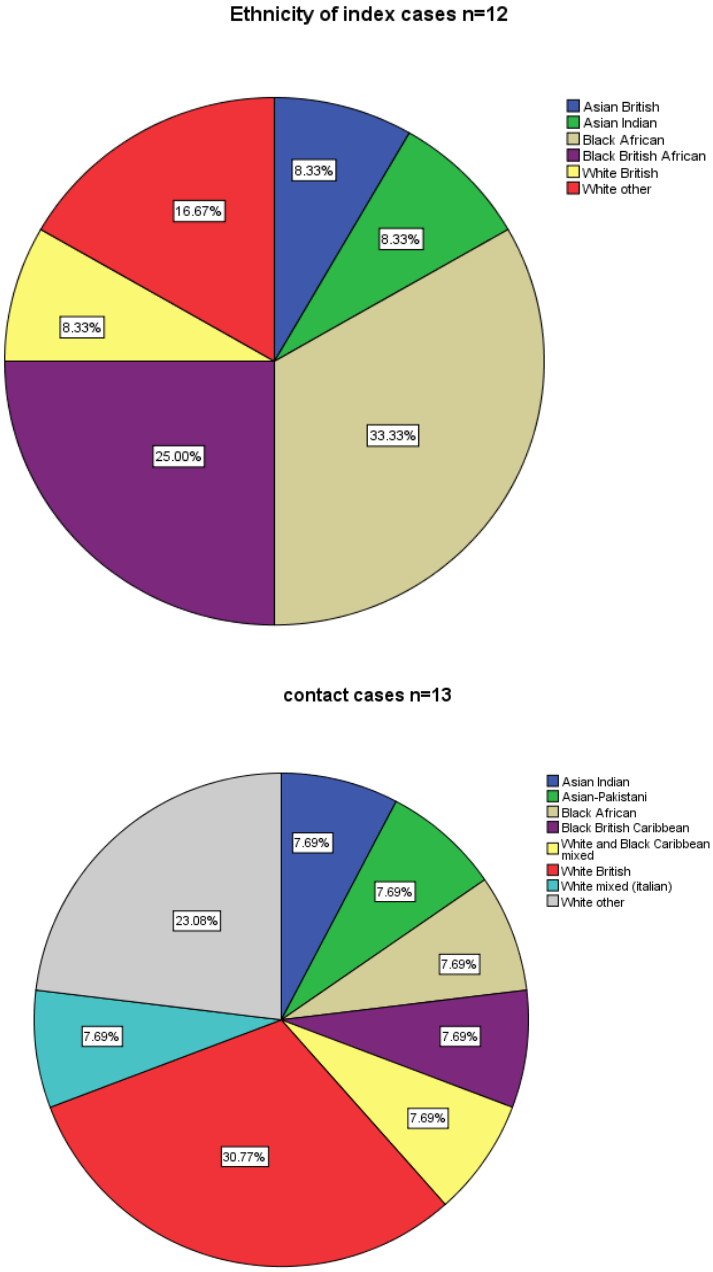
Demographics	Index cases	Contact cases
Female	24	48
Male	23	31
Average age	33	36
Age range	19-70	18-61

Table 29: Ethnicity of all patients and contacts screened

Ethnicity	Index cases	Contact cases
Black African	23	24
British Black African	3	9
White British	4	22
White other	4	14
Indian Asian	2	5
Black British Caribbean	2	4
Mixed	6	1
British Asian	1	0
Asian other	1	0
Asian Bangladeshi	1	0

Table 29 shows the overall characteristics of all the patients who were approached to take part and reflect a typical TB population, i.e. a high prevalence of Black African index cases and few White British cases. One can see that the White British cases are more predominant in the contact group.

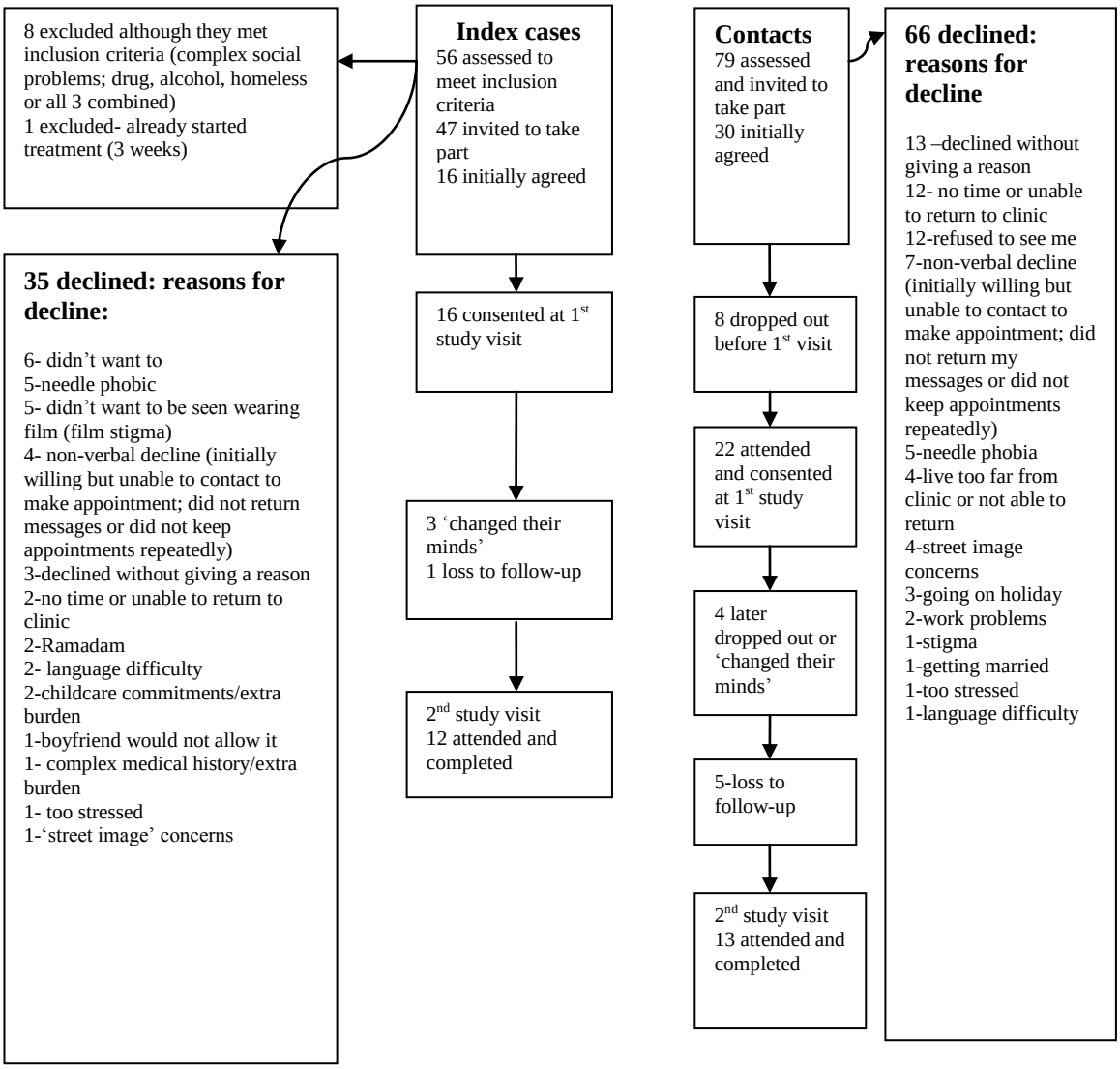
Figure 27: Demographics of subjects who completed the study



The pie charts show the demographics of the sample that completed the study. The index group comprised of 12 cases, with 33% of the group being Black African, followed by Black British African, at 25%. The contact group, however, shows a slightly different distribution, with the largest slice reflecting White British and White Other groups as the greater proportion of ethnic spread (31% and 23% respectively).The index group consisted of 6 females and 6 males, with an average age of 33. The contact group comprised of 6 males and 7 females, with an average age of 38.Only 12 index and 13 contact cases completed the study, one index case

recruited last, later dropped out from the 13 who originally agreed. Of those patients and contacts who did complete, most required a great deal of contact and encouragement over the monitoring period, in order to ensure that they returned for a second visit. Many required numerous telephone calls and there were many who repeatedly did not attend appointments they had made. Figure 28 shows the flow of patients through the study and the reasons subjects gave for declining.

Figure 28: Allocation and inclusion plus reasons why subjects did not take part



Of the index cases that completed the study, 6 had pulmonary Tuberculosis; 3 lymphatic; 1 had Tuberculosis of the fallopian tube; 1 had an infected abscess and 1 of the menigeal membranes. Of the pulmonary cases, 4 were culture positive and 1 was smear positive. Of the index cases, 7 were reactive to IGRA, 1 was negative and 1 result was equivocal, according to the laboratory reference range. 1 contact case was

reactive to IGRA, but was later found to have latent Tuberculosis, for which she was treated.

7.8.3 Compliance with Polysulphone film use

When patients returned for their last study visit they were asked whether they had forgotten to wear the film when outside on any of the monitoring days, whether they had travelled abroad and monitored their exposure in a different environment outside London and whether they had worn the film on the site instructed (lapel) or at a different site on the body. Only 1 subject reported that he had missed a day of monitoring over the eight week period and 1 subject had chosen to wear the film on a hand bag rather than the lapel site, as it was more convenient. 1 subject, with surprisingly high exposure levels, had worn the film at a summer music festival during a sunny weekend. Many of the subjects did not return the films, as they had lost or 'forgotten' them on return to clinic. Table 30 below details the fate of the films in the monitoring groups.

Table 30: Reasons why films were not returned in study subjects

	Lost	Did not return	Refused to wear	Returned 1 of 2	returned
Index	2	3	1	1	5
Contacts	4	0	0	0	9

Of the index cases, 3 subjects did not return the films for reasons that were not easily explainable, or they reported that they would later return them in the post but failed to do so. 2 subjects reported that they had lost the films and that they had dropped off their clothing during the monitoring period. 1 subject was recruited, but later reported that he did not wish to wear the films as instructed and, therefore, did not return the unexposed films. 1 subject returned only 1 film. Only 5 of the 12 index cases returned their films. Of the contact cases, 4 reported losing the films and 9 returned them.

7.8.4 Factors affecting the quality of the returned films

Of the films that were returned, there were some quality issues that may have affected the accuracy of the reading taken from the film. The condition of some of the films

can be viewed in Figure 29. These included films that had become contaminated with clothing fibres and grease, and kinked films as illustrated below. One subject in the index group had stuck a small transfer on the film to amuse his children. Obstruction of the film surface is likely to reduce its potential for exposure, and damaged films, in the ways described here, have been shown to increase the read out Polysulphone film leading to artificially high values(217).

Figure 29: Film condition on return to clinic after 8 weeks

7.9 Question 1. What is the contribution of sunlight to 25 (OH)D status in active TB cases and contacts?

The research question this study sought to address was the contribution of sunlight to vitamin D status. I shall first describe the differences in Vitamin D status between the groups before going on to explore the other factors that had significance to Vitamin D status including the UVR exposures of subjects in both groups. The difference in Vitamin D in both groups, pre and post monitoring is described overleaf. The box plot (Figure 30) shows baseline Vitamin D and changes in Vitamin D status following the 8 week monitoring period. The thick lines in the centre of the box plot show median values whilst Table 31 displays the mean values.

Figure 30: Changes in 25(OH)D over 8 weeks from recruitment to final study visit in index and contact cases

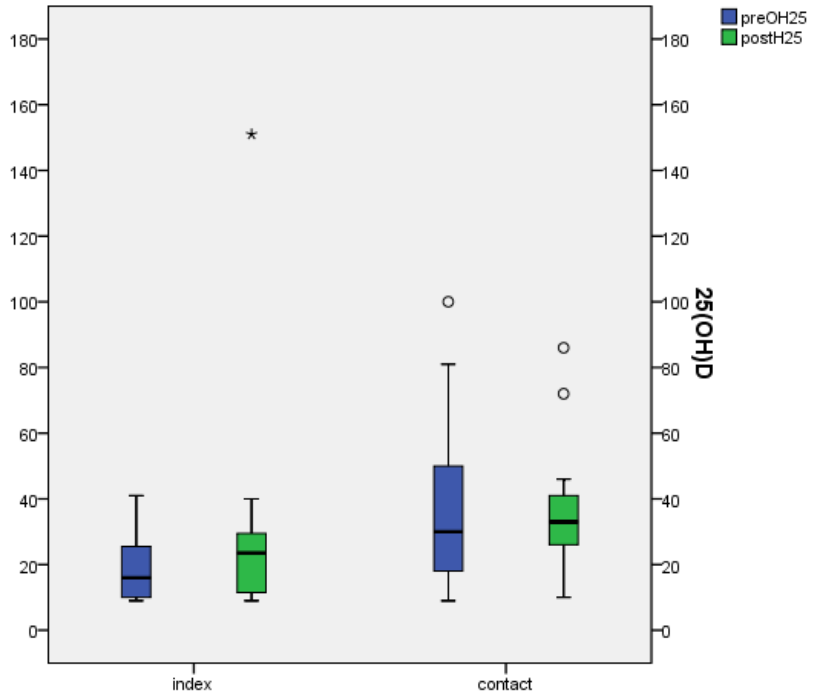


Table 31: Changes to 25(OH)D status over monitoring period

Index and contact cases			Baseline 25(OH)D nmol/l	Post monitoring 25(OH)D
contact	N	Valid	13	13
		Missing	0	0
	Mean		38.46	36.15
	Std. Deviation		28.430	21.882
	Range		91	76
index	N	Valid	12	12
		Missing	0	0
	Mean		18.75	31.67
	Std. Deviation		10.481	38.869
	Range		32	142

The mean for the index group was 18.75 nmol/l prior to monitoring and 31.6 nmol/l at the final study visit. The contact group showed a mean value of 38.4 pre monitoring and 36.1 post monitoring. There was no significant difference between the mean levels of index and contact cases at the beginning of the study or at the final study

visit. An independent sample Mann-Whitney U test was computed to test the significance of the difference between groups for Vitamin D status pre and post monitoring (pre=0.080 and post=0.097, p=0.05). A non parametric test was selected due to the very small sample size. Figure 31 shows the results of the test.

Figure 31: Results pre and post significance testing before and after monitoring

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of preOH25 is the same across categories of indexcont.	Independent-Samples Mann-Whitney U Test	.080	Retain the null hypothesis.
2	The distribution of postH25 is the same across categories of indexcont.	Independent-Samples Mann-Whitney U Test	.097	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

What was most striking was the degree of deficiency and insufficiency evident in both the index and contact groups. Deficient, insufficient, adequate and optimal ranges were judged according to a recent consensus statement for optimal bone health(218). Deficiency was judged to be levels < 25 nmol/l, levels between 25-50 nmol/l were judged to be within the 'insufficient range, levels between 50-70 nmol/l are said to be 'adequate' whilst levels >75 are defined as 'optimal'. In the index group there was a slight elevation to the levels obtained at the second visit, with no significant change in levels noted in the contact group. There was 1 notable outlier in the index group with very high levels (151nmol/l). This subject was identified as being profoundly Vitamin D deficient through independent clinical assessment and commenced on high does Vitamin D by the GP. By the end of the study, this deficiency had been corrected and the subject achieved these high 25(OH) D levels as a result. This skewed the data in the second measurement of the index group, as evident in the histograms. The other subjects were advised to consult with their GP.

Having described the overall findings in relation to the Vitamin D status of both groups, I should now like to examine, in some detail, the relationship of other important factors that have been described earlier in this thesis, to examine their relative importance to the Vitamin D status of both groups.

7.9.1 The season of monitoring

Table 32 and Table 33overleaf provide an overview of the raw data and its relation to season, months and years of recruitment, and monitoring of both index and contact cases. In the index group, 8 subjects were recruited at times of the year where the literature reports potentially enough ambient UVR in the UK (providing subjects are exposed; 6-10% body surface) to generate cutaneous vitamin D(207;219). In the contact group, 11 subjects were recruited at such times. Vitamin D 'friendly' months are indicated by a sun symbol and the winter snow symbol in the tables indicates times/months reported where there is not adequate ambient UVR to support Vitamin D synthesis in the skin(218). It is also widely reported in the literature that, from November and through February in the UK, there is insufficient ambient UVB to promote vitamin D synthesis in the skin, to the order that is deemed optimal, or that the required exposure time to achieve such levels would be impractical. (9/13) 69% contacts showed deficient or insufficient Vitamin D status in Vitamin D friendly months as did (8/12) 67% of index cases. In the contact group there were no cases that managed adequate or optimal Vitamin D status in winter months and only 1 in the index group. However, this subject was heavily supplemented. Vitamin D levels in the deficient range (<25 nmol/l) can manifest in clinical Rickets or Osteomalcia in adults. Levels between 50-75 are said to be adequate with levels > 75 being optimal for bone health(218). The results here suggest that, regardless of season, both groups have an inclination towards Vitamin D deficiency, not just the Tuberculosis group.

Table 32: Index cases displaying season, month and year of recruitment related to Vitamin D status before and after monitoring period

Index Case	Date of monitoring	Season	Vitamin D potential	Baseline 25(OH)D nmol/l	Post 25(OH)D nmol/l	25(OH)D Status at end of study
1	06.03.10-26.04.10	Spring		18	15	Deficient
2	26.05.10-04.08.10	Summer		10	<10	Deficient
3	21.06.10-11.08.10	Summer		33	26	Insufficient
4	02.11.10-18.01.11	Winter		12	<10	Deficient
5	02.12.10-09.02.10	Winter		<10	21	Deficient
6	23.07.09-21.09.09	Summer		41	30	Insufficient
7	31.07.09-21.09.09	Summer		17	40	Insufficient
8	27.01.10-22.03.10	Spring		10	14	Deficient
9	04.03.10-04.05.10	Spring		<10	<10	Deficient
10	09.03.10-21.06.10	Spring/summer		15	27	Insufficient
11	22.12.10-25.02.11	Winter		28	151	Optimal*
12	19.01.11-16.03.11	Winter/spring		23	29	Insufficient

* Subject received Vitamin D supplementation

Table 33: Contact cases displaying season, month and year of recruitment related to Vitamin D status before and after monitoring period

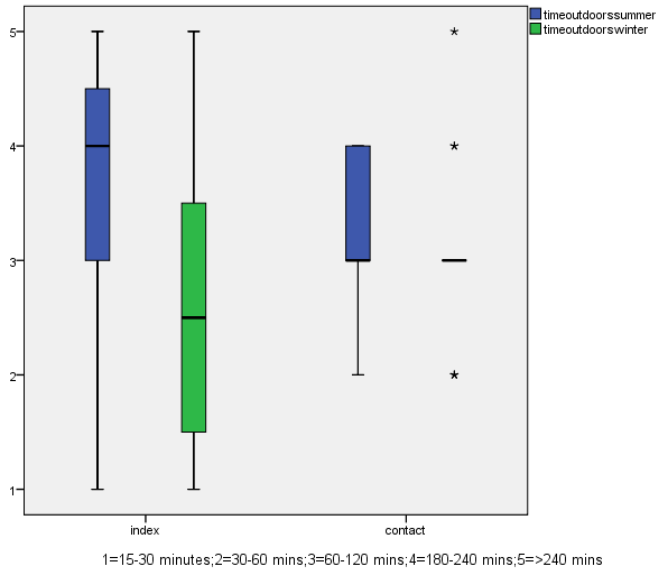
Contact Case	Date of monitoring	Season	Vitamin D potential	Baseline 25(OH)D nmol/l	Post 25(OH)D nmol/l	25(OH)D status at end of study
1	15.02.10-12.04.10	Winter/spring		46	33	Insufficient
2	21.01.10-26.03.10	Winter/spring		18	19	Deficient
3	16.02.10-14.04.10	Winter/spring		30	26	Insufficient
4	03.03.10-03.06.10	Spring/summer		<10	11	Deficient
5	29.04.10-13.07.10	Spring summer		50	46	Insufficient
6	08.05.10-21.07.10	Spring/summer		25	72	Adequate
7	02.07.10-28.08.10	Summer		28	30	Insufficient
8	09.07.10-16.09.10	Summer		100	86	Optimal
9	05.08.10-27.09.10	Summer/autumn		61	36	Insufficient
10	07.08.10-12.10.10	Summer/autumn		34	27	Insufficient
11	19.09.09-01.12.09	Autumn/winter		<10	33	Insufficient
12	07.10.09-17.12.09	Autumn/winter		81	41	Insufficient
13	09.10.10-01.02.11	Winter		<10	10	Deficient

7.10 Question 2. Is Vitamin D deficiency in index cases and contacts explained by differences in sun exposure and other factors that influence Vitamin D status?

7.10.1 Time spent outdoors

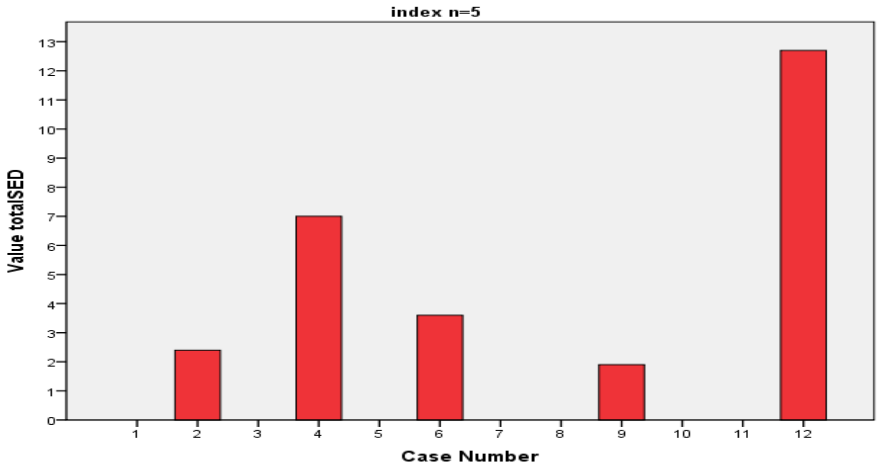
I would now like to examine in more detail the other factors that affect Vitamin D status and determine their contribution to the Vitamin D status of the sample.Time spent out doors is crucial if any radient exposure is to be achieved. The time people spend outdoors has been shown to vary, according to seasonal behaviour, lifestyle and temperate conditions(205). City life often dictates that people spend little time outside and, when they do, the potential for UV exposure can be hindered by shadowing from buildings and trees(189). In order to determine the average time spent outside, each subject was asked on the first visit, on average, how long they spent outdoors per day in summer, in winter and over the last two months(Appendix 7). The box plots in Figure 32 provide the data reported from both groups.The y axis labelled 1-5 represents the time frames from 1-15-30 minutes only; 2-30-60 mins; 3-60-120 mins; 4-180-240 mins and 5-> 240 mins.The contact group reported that, in the summer the majority spent between 30-60 minutes and 180-240 minutes outside in daylight hours, with some spending much less time and some much more. Winter exposure in this group shows that the subjects reported spending more time indoors.

Figure 32: Index cases: Time spent outdoors during summer and winter in index and contact cases



The index group reported spending more time outdoors when compared to the contact group, with some difference reported between winter and summer exposures. Figure 33 and Figure 34 summarise the Polysulphone film measurements of those who returned the films, and reflect cumulative doses over the 8 week period.

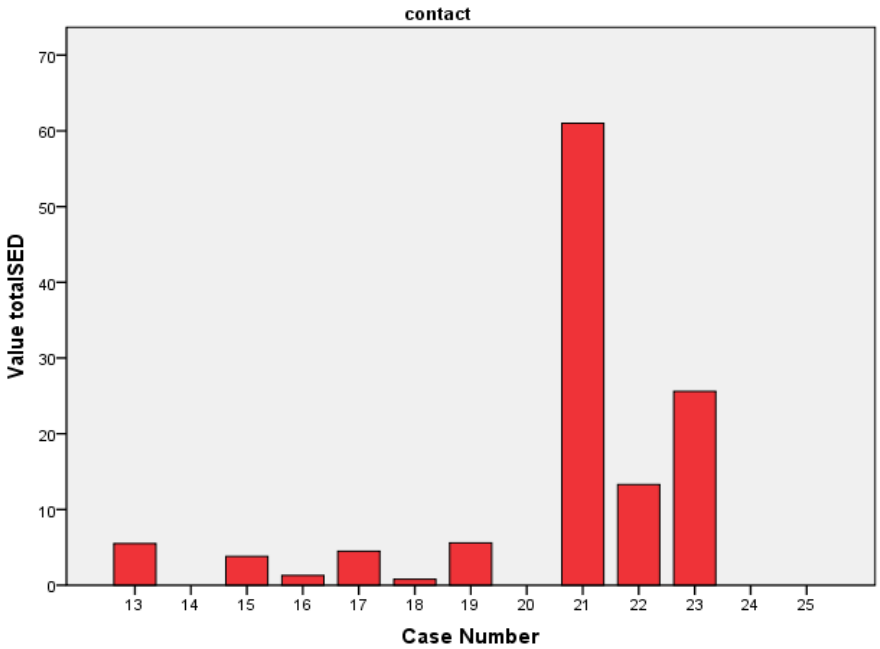
Figure 33: SED values of index cases who returned PS film. Measurements = 8 weeks exposure



Sum of SED of returned films from the index cases

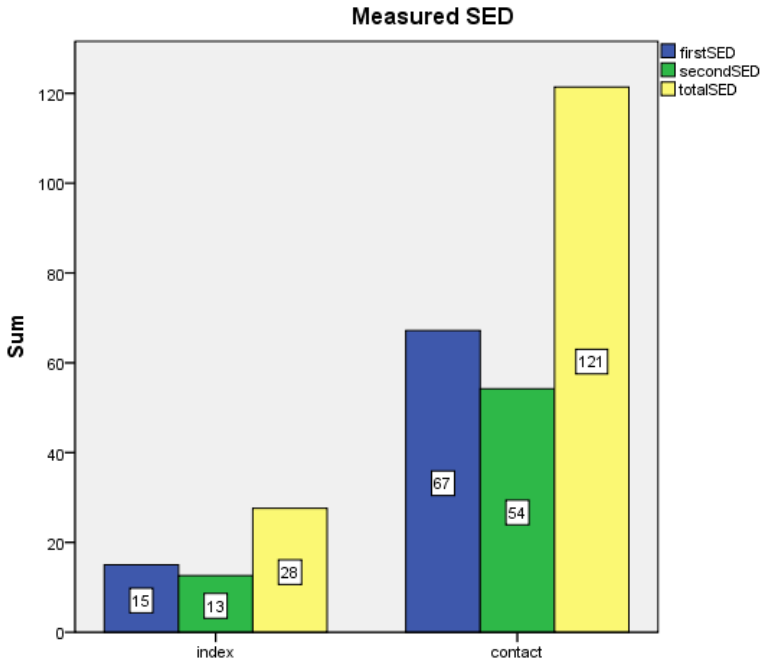
SED= Standard Erythemal Dose.

Figure 34: SED values of contact cases who returned PS film. Measurements = 8 weeks exposure



Sum of SED of returned films by the contact cases

Figure 35: Sum of SED calculated from returned films by group



Measured SED over study period for both index and contact groups

Figure 35 shows the total measured SED of those subjects who returned the films. The contact group show a much greater exposure over the 8 week period. The blue bars represent SED over the first four weeks of the monitoring period, the green bar represents the second four weeks and the yellow bar provides the sum of SED over the two months of monitoring. The contact group shows proportionally higher sun exposure than the index group although reported less time spent outdoors. A Spearman's rho correlation was computed to determine the strength of the relationship between time outdoors and SED, time outdoors and 25(OH)D status and finally, 25(OH)D and SED. In contact cases, time outdoors and SED showed a moderate positive association: (r=.487) but did not achieve significance (sig=0.108,p=0.05). In contact cases, this relationship was moderately weak: (r=.313), but also did not achieve significance (sig=0.298,p=0.05). The relationship between time outdoors and 25(OH)D was weakly correlated in the index group: (r=.022, sig=0.947,p=0.05). In contact cases, these variables showed an inverse relationship but did not achieve the significance level (r= -.056, sig=0.85,p=0.05). Finally, there was no association between 25(OH)D status and SED in the index group (r=0.016, sig=0.961,P=0.05) and a weak positive association in the contact group between these two variables(r=.233,sig=0.44,p=0.05).

7.10.2 Calculating sunlight exposure

As so few subjects returned the films, I was unable to use these to calculate the daily SED for most subjects. I, therefore, had to resort to an alternative method that took data gathered in the questionnaires and used these to calculate the daily SED to the skin areas exposed, by application of an equation described by Diffey(205;206).

$$Daily\ exposure = UV \times EF \times \left[1 - \left(1 - \frac{h}{H}\right)^2\right] SEDs$$

UV is obtained from published tables. It is the mean daily ambient ultraviolet insolence by latitude and month, measured at Chilton by the Radiological Protection Board during the years 1991-2004, using erythemally weighted detectors(207). The solar response of these instruments mirrors very closely the International Commission on Illumination (CIE) reference erythemal action curve(220). EF is the fraction of UV that irradiates the exposed body sites such as the forearms, legs, arms, face and hands when the body is exposed to UVR. The literature reports EF to range between 20%-60%(221). For the purposes of this study, an exposure fraction of 0.2 was assumed, as this conforms to the average determined by personal monitoring studies. *h* is time spent outdoors and assumes that this is symmetrically distributed either side of solar noon. *H* is the number of daylight hours per month at the latitude of interest, reported by: http://www.orchidculture.com/COD/daylength.html

In this study, exposure of hands and face was taken to be approximately 6% of skin exposed; + short sleeve shirts = 20%; + shorts or skirt exposed 40%; + swimsuit exposed 80%. These variables were assessed with the help of a picture card that was included in the questionnaire for subjects to identify. Sunscreen use was also factored into the calculation by the following process: Effective sun protection factor (SPF) was calculated by dividing the manufacturer's SPF claim by three. This was adopted by Diffey et al as a means of correcting for behavioural factors such as variation in efficacy of application(222;223). This approximately provides the *effective* SPF(224). The mean daily ambient erythemal UV (in SED) was calculated by dividing the monthly Chilton measures by 30(207). One SED is a standardised measure of erythemal UV and is equivalent to an erythemal effective exposure of 100 J/m²(181). An exposure of 3-4 SED is required for a minimal erythemal dose on previously unexposed buttock skin in the most common British skin types (II/III)(225). It has

been claimed that abundant synthesis of Vitamin D is reported to occur well below this point.

Table 34 and Table 35 show the results of SED values received by the sample over the monitoring period, according to the methods described by Diffey. Personal exposure data, skin type, and time spent outdoors were entered into an excel database that was programmed to calculate daily exposure dose. Column 8 provides the daily exposure SED as calculated by equation 1. Both tables provide the raw data, % body area exposed, skin type, season, mean ambient UVR (as previously described) and the calculated skin area exposure in % SED and finally, the Vitamin D status of the subject. The % SED is a product of column 8 by the % of skin area exposed (column 3). 42% of the index group and 46% of the contact group received an exposure dose of 5% and above, an approximation of Vitamin D producing energy, assuming skin type 2-3. Vitamin D deficiency and insufficiency was prevalent in both index and contact groups regardless of receiving doses estimated to provide sufficient Vitamin D. The estimation, a product of daily exposure (equation 1) and skin area exposed (column 3) proposed by Diffey was based upon a commonly quoted standard that states that: if *" 6-10 % of the body surface is exposed 2 to 3 times a week to the equivalent of about 5 minutes of Boston midday summer sunshine in the spring, summer and autumn; this should be more than adequate to satisfy the body's requirement for vitamin D throughout the year"*(219). This is so often quoted in the literature that a recent paper has named this proposition 'Holick's rule'(226). This irradiance is equivalent to 6 SED/h; 5 minutes exposure will result in 0.5 SED, so the skin area exposure dose (assuming the minimal exposure 6- 10% of body area exposed) is 5 %SED(204).This degree of exposure is reported to generate a dose equal to 1,000 IU of Vitamin D. Those subjects who received the required skin exposure dose of 5% and above are indicated in red in both tables in column 9. Assuming that subjects reported accurately their time outdoors and dress style, a significant proportion of subjects in both groups failed to achieve adequate or optimal levels. Additionally, this included subjects with pale skins who, according to this model, should have achieved adequate levels.

Table 34: SED values for index cases per day according to reported time outdoors, % body exposed, and mean daily ambient UVR

index	Time outdoors	% body exposed	Skin type	Month monitoring	Mean ambient SED	Fraction daily ambient UV	Skin exposure in SED	Skin area exposure dose % SED per day	Exposure as % ambient	25(OH)D_3	SED of returned film (total)	Sunscreen use
1	4 hours	6	5	Aug-Sept	10.4	0.54	1.12	**6.7***	0.8	30 insufficient	13	Never
2	3-4 hours	20	6	Aug-Nov	1.4	0.74	0.21	4.2	14.9	40 insufficient	DNR	Never
3	<1	6	3	Jan-March	5.6	0.32	0.36	2.1	6.4	14 deficient	3.6	Occ
4	< 4	6	5	March-May	18.2	0.44	1.60	**9.6***	8.8	<10 deficient	DNR	Never
5	3-4	6	3	March-May	18.2	0.44	1.60	**9.6***	8.8	15 deficient	7	Never
6	3-4	6	3	March-June	22.8	0.41	1.88	**11.3***	8.3	27 deficient	DNR	Never
7	3-4	6	5	April-June	22.8	0.41	1.88	**11.3***	8.3	<10 deficient	2.4	Never
8	< 1	6	3	June-Aug	18.9	0.13	0.50	3.0	2.6	26 deficient	DNR	Never
11	3-4	6	4	Nov-Jan	0.7	0.78	0.12	0.7	15.6	<10 deficient	DNR	Never
12	<1	6	6	Oct-Feb	2.0	0.20	0.08	0.5	4.0	21 deficient	DNR	Never
14	1-2	6	6	Dec-Feb	2.0	0.30	0.15	0.15	0.9	151 optimal	1.9☺	Never
16	<1	6	5	Jan-March	5.6	0.17	0.09	0.6	1.7	29 deficient	DNR	Never

Values calculated from month of second visit to reflect vitamin D synthesis over the previous two months

If reported time outdoors is < 1, the value entered =1 hour

Time outdoors used to calculate the skin area exposure dose per day was taken from the season of exposure, I.e. if a subject reported spending 1-2 hours outdoors per day in the summer and they were monitored in the summer, the summer values were entered rather than the winter values.

Ambient average daily SED taken from Chilton data(207).

***Values highlighted in red show skin area exposure dose at 5% and above; proportion of daily exposure estimated to be sufficient to maintain Vitamin D sufficiency.

Table 35: SED values for contact cases per day according to reported time outdoors, % body exposed, and mean daily ambient UVR

contacts	Time outdoors	% body exposed	Skin type	months	Mean ambient SED	Fraction daily ambient UV	Skin exposure in SED	Skin area exposure % dose SED	Exposure as a % ambient	25(OH)D_3 nmol/l	SED of returned films (total)	Reported sunscreen use
1	1	6	5	Aug-Dec	0.6	0.27	0.03	0.2	5.4	33 insufficient	DNR	Never
4	1-2	6	4	Feb-April	10.6	0.27	0.58	3.5	5.4	33 insufficient	4.5	Always
5	1-2	6	3	Jan-March	5.6	0.32	0.36	2.1	6.4	19 deficient	1.3	Always
7	1-2	20	3	Oct-Dec	0.6	0.50	0.06	1.2	9.9	41 insufficient	3.8	Often
8	3-4	6	4	April-June	22.8	0.41	1.88	**11.3***	8.3	26 insufficient	DNR	Never
9	3-4	6	6	March-June	22.8	0.41	1.88	**11.3***	8.3	11 deficient	5.5	Never
10	3-4	20	4	April-July	22.6	0.40	1.91	**38.3***	8.5	46 insufficient	DNR	Only when sunbathing
12	3-4	6	3	May-July	22.6	0.42	1.91	**11.5***	2.6	72 adequate	26	Occ
14	1-2	20	5	July-Sep	10.4	0.30	0.61	**12.3***	5.9	30 insufficient	13.3	Never
15	1-2	40	2	July-Sept	10.4	0.30	0.12	4.9	1.2	86 optimal	61 ☺	Always SPF 30
16	3-4	6	2	Aug-Sept	10.4	0.54	0.11	**6.7***	8.5	36 insufficient	5.6	Often SPF 20
17	4	20	5	Oct-Dec	0.6	0.82	0.10	2.0	16.5	27 insufficient	DNR	Never
19	1	6	5	Dec-Feb	2.0	0.20	0.08	0.5	4.2	10 deficient	0.8	Never

* Skin area exposure dose of 5% and above has been postulated to be sufficient for the body's Vitamin D requirement year round, assuming 6-10% body exposure (face and hands) to midday summer, spring and autumn sun. Mean ambient measurements taken from month when monitoring ended.

DNR= did not return (films).

Table 36: Index cases showing actual SED measurements for subjects who returned films, Vitamin D status, and skin area exposure dose

Skin type	Skin area exposure dose %SED	Vitamin D status	Daily SED from PS film
5	6.7*	30 insufficient	**0.2**
3	0.6	14 deficient	**0.07**
3	7.5*	15 deficient	**0.12**
5	8.7*	<10	**0.03**
6	**0**	**151**	**0.03**

Table 37: Contact cases showing actual SED measurements for subjects who returned films, Vitamin D status, skin area exposure dose

Skin type	Skin area exposure dose % SED	Vitamin D status	Daily SED from PS film
5	0.1	33	**0.08**
4	1.8	33	**0.10**
3	0.6	19	**0.01**
3	0.3	41	**0.07**
6	8.7*	11	**0.10**
3	13.4*	72	**0.46**
5	6.4*	30	**0.23**
2	12.8*	86	**1.08** ☺
5	**0.0**	**10**	**0.01**

☺ denotes the only subjects who received sufficient daily SED to achieve optimal levels

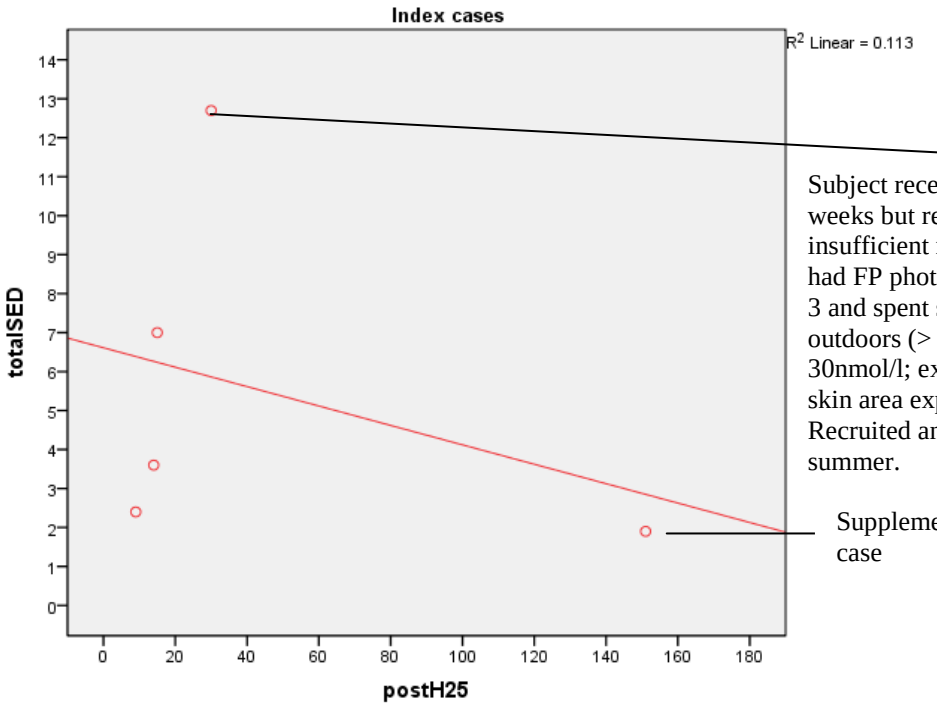
7.10.3 SED measurements from PS film compared with estimated exposure

Table 36 and Table 37 show the measured SED of those who returned the films after the 8 week monitoring period. We can adopt a very crude method to estimate a daily SED received for those subjects by dividing each total by the number of days monitored. The result would approximate the daily SED each subject received. If we examine the results presented in the tables following this simple calculation, it becomes evident that on a daily basis, exposure to UVB was extremely low, and in most cases, did not reach 1 SED per day. Even those with paler skins showed low levels of Vitamin D, which suggests that the Diffey approach, of estimating Vitamin D producing energy may over estimate exposure, for those living and working in an urban setting.

7.10.4 Relationship between SED calculated from PS films and Vitamin D status

Figure 36 and Figure 37 show the relationship between Vitamin D status (last visit) and total SED of those subjects who had returned the films from which a measurement was taken. It is interesting to note the difference in the patterns of these data in both index and contacts. Examining these data as case studies, it may be possible to detect 'signals' that indicate the direction of the relationship by individual scrutiny. Immediately, it became apparent that there were visual differences in these variables, between the groups. In index cases for example there was no relationship between SED and Vitamin D levels (R^2=0.113). In contact cases however, there was a relationship (R^2 = 0.776). As time outdoors was taken from the season of monitoring, time spent outdoors during the monitoring period was comparable (34 hours index cases and 36 hours in contacts, on average per day). In the index group there was one case, which regardless of receiving the highest exposure levels remained Vitamin D deficient. The subject identified in figure 34, received a total of 13 SEDs over the monitoring period, a skin area exposure dose of 6.7%, which is above the level estimated as adequate to generate Vitamin D. This subject was recruited and monitored in summer, when ambient UV is high. If we assume that Diffey's predictors are correct as a rough guide to Vitamin D radiant energy received, this could support the hypothesis that this case was compromised in his ability to synthesise Vitamin D. What could be the reason for this? The possibility of inaccurate reporting by the subject as a cofounding factor is contradicted by the high personal film measurements. The SED measurements of the films returned indicated significant exposure to UVR energy, a total of 1,300 jm², but in this case, it was not enough to generate optimal levels of Vitamin D.

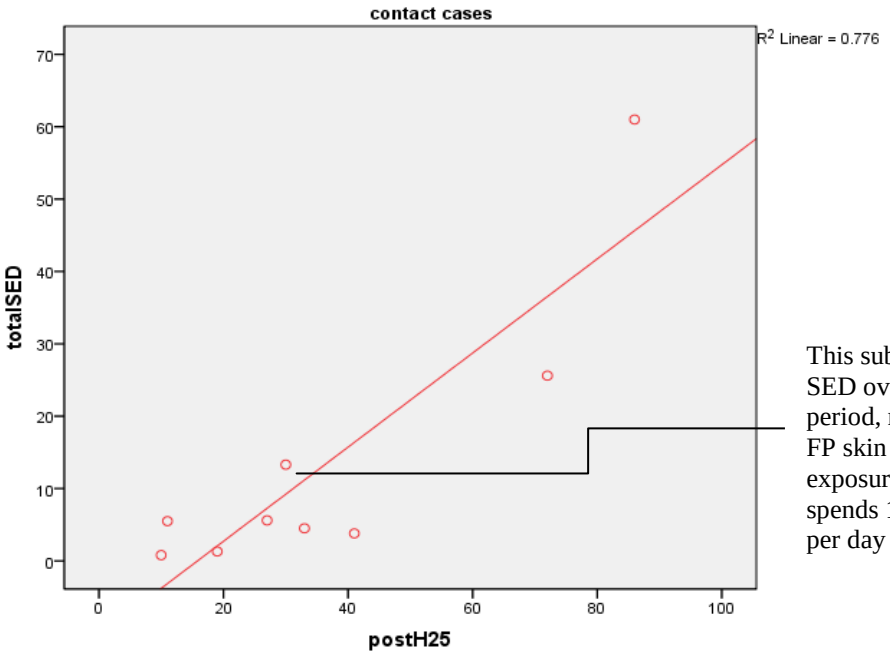
Figure 36: 25(OH) D of index cases who returned films and total SED received over the monitoring period. n=5



Subject received 13 SED over 8 weeks but remained in the insufficient range. This subject had FP photo-type 5; Diffey type 3 and spent significant daily time outdoors (> 4 hours). 25(OH) 30nmol/l; exposure fraction 6%; skin area exposure dose 6.7%. Recruited and monitored in summer.

Supplemented case

Figure 37: 25(OH) D of contact cases who returned films and total SED received over the monitoring period. n=9



This subject received 13 SED over monitoring period, recruited in summer; FP skin type 5; skin area exposure dose SED 12.3%; spends 1-2 hours outdoors per day

Following close examination of the contact cases who returned their films, another intriguing phenomenon emerged: there was one case who, regardless of high SED (13), summer recruitment and a skin area exposure dose of 12.3%, above that estimated as the level where Vitamin D status should be adequate, displayed Vitamin D insufficiency. This is an unexpected finding. What is interesting is that this subject also displayed a positive response to the IGRA and was found to have latent Tuberculosis and, therefore, was not an unaffected contact. This subject was treated with Chemoprophylaxis. The subject reported skin type 5 and this may have been a significant factor in her Vitamin D insufficiency. The potential for skin types to affect Vitamin D status is reported in the next section. This case study may signify however, that those patients with latent disease are also susceptible to a greater degree of Vitamin D deficiency than healthy controls, who possess similar confounding factors. It may also indicate that Vitamin D status in those infected with *Mycobacterium Tuberculosis,* and those with active disease, is not associated with UV exposure. However, much larger samples would be required to test this hypothesis.

One cannot ignore the impact of skin colour on these results. If we examine the relationship between photo-reactivity of the skin and the Vitamin D status of subjects in more detail, assuming that Diffey's model was more sensitive for fair skin types, anomalies still appear. For example, in the index group, 2 subjects received the required radiant dose and had skin types that should predict adequate Vitamin D synthesis (2-3), yet were still severely deficient or bordering on deficient. One subject in the index group had optimal levels, regardless of season and skin type 6, but was medically supplemented. In the contact group one subject with skin type 2 received sufficient skin area exposure dose yet did not achieve sufficient or optimal levels. This subject did report often using a factor 20- sunscreen and this may have been significant to the result. Of the other subjects in this group whom achieved sufficient exposure but did not manage to generate healthy Vitamin D levels, all had darker skins. 1 subject in the contact group achieved optimal levels of Vitamin D but also received the highest sun exposure (1.08 SED per day).

7.10.5 Did skin colour explain Vitamin D status?

In the method selection and pilot testing chapter, I described two methods of classification of photo reactive skin types and the potential problems of using self-

reported measures as an objective indicator of skin colour and behaviour. To my knowledge there are no other studies that have employed objective skin colour measurements and related these to Vitamin D status in a group with Tuberculosis. To mitigate possible inaccuracies in reporting I employed both self-classifications scales of photo type and an additional objective method as earlier described. The self-reported scales are used here for descriptive purposes, given that I did not achieve a powered sample in which they could be compared.

Table 38: Photo-reactive skin type in index cases and contacts

Fitzpatrick skin type	Index group	Contact group	Diffey Skin type	Index group	Contact Group
1	0	0	1	1	3
2	0	2	2	5	6
3	4	3	3	6	4
4	1	3			
5	4	4			
6	3	1			

Table 38 shows the frequency of self-reported skin type using both Fitzpatrick and Diffey scales as reported by the subjects on their first study visit. The index group reported slightly less photo-reactivity than the contact group that included paler skinned subjects with greater photo-reactivity reported (paler skin that frequently burns and never tans).

Figure 38: Relationship between constitutive melanin and photo-type according to Diffey in index and contacts

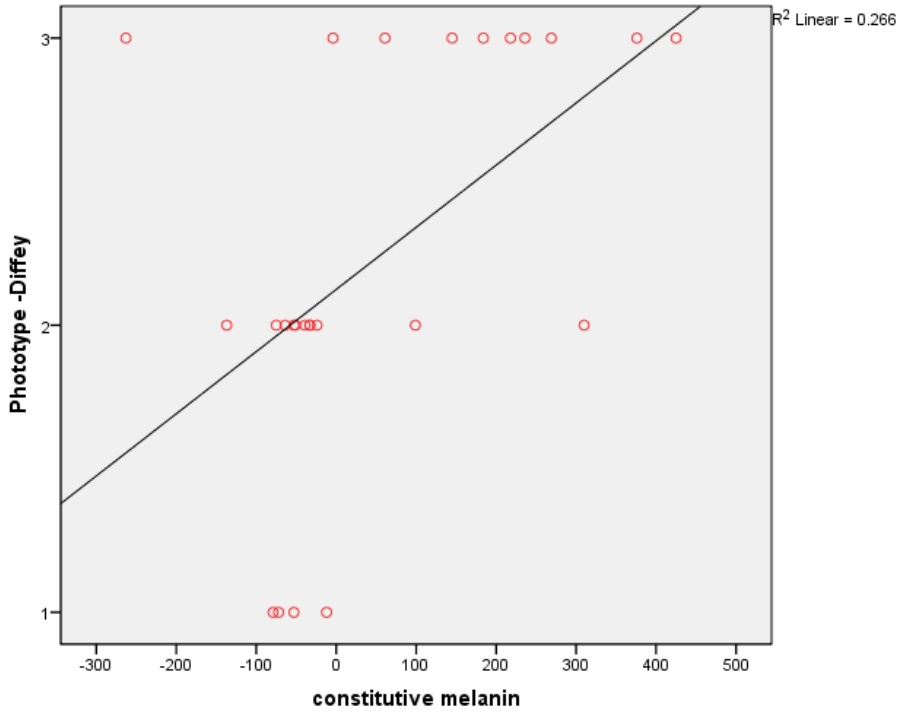


Figure 38 shows how the Diffey scale correlated to the melanin measurements when both index and contact subjects are considered together. There is not a clear linear relationship between these data points. However, it might be that the scale used in the scatter plots is too narrow and if these values were plotted against the entire dynamic range of the melanin metre, a more linear pattern would appear. The data range for skin type 3, for example, is -330 to + 450 which, although seems like a wide spread the actual range of possible measurements of the metre is -999 to +999.

Figure 39: Relationship between constitutive melanin and Fitzpatrick photo-type in index and contacts

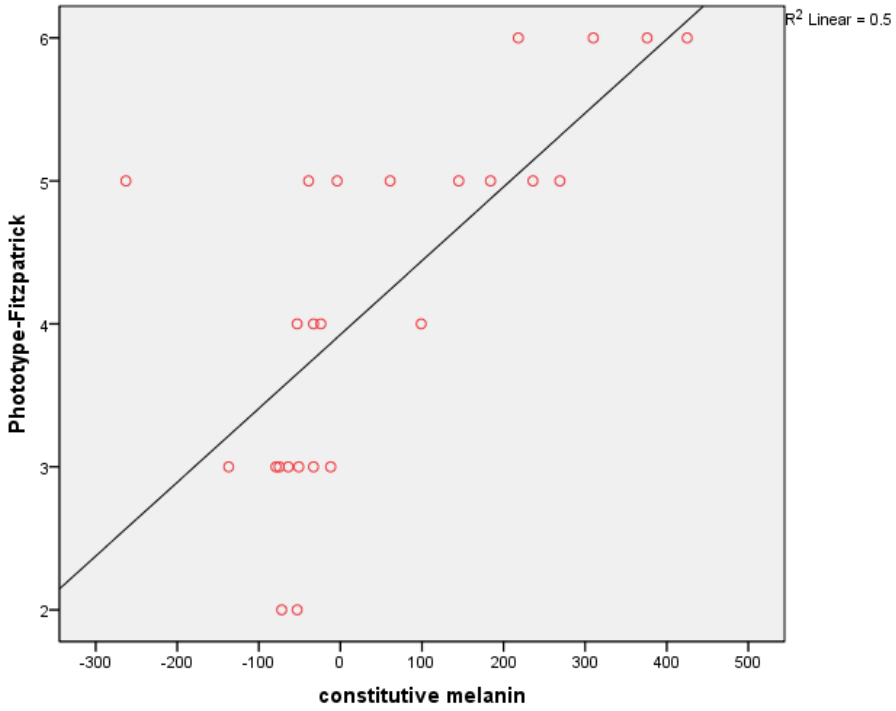
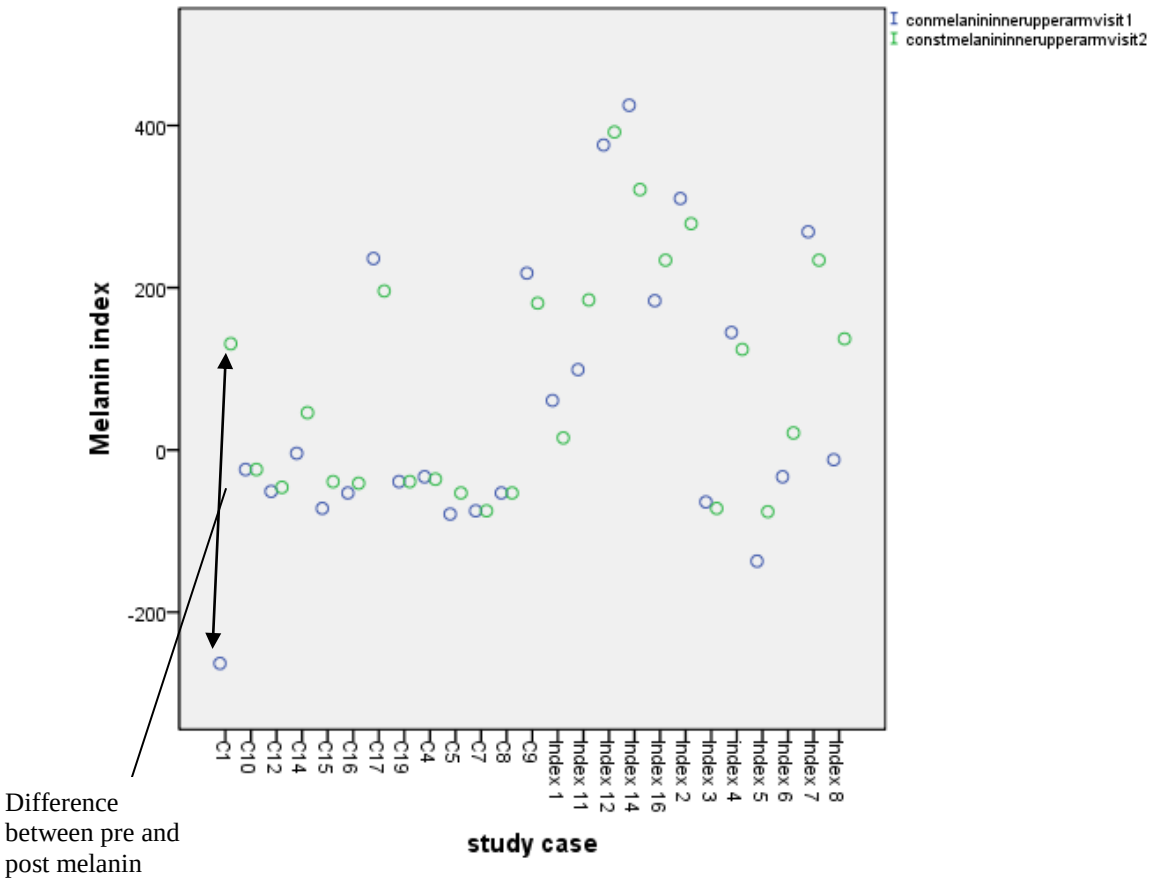


Figure 39 shows the relationship between the melanin index and the Fitzpatrick scale of both index and contacts. One can see that the visual relationship of the data is again quite spread out, with a wide range of measurements evident within each of the skin categories. The 4 subjects, for instance, who described their skins as very dark and never burning, had melanin index measurements between a range of 200-450, which is relatively narrow measurement range. However, there was greater range in measurement reported for skin type 5, ranging from -200-+290. Using the Diffey scale, the range in the darker group (skin type 3) is much greater, with data ranging from -290-+450.With the very small number of subjects, however, it is difficult to draw any significant inferences from these results, other than to describe the properties of the subject's skin.

Figure 40: Changes in constitutive melanin in subjects over 8 weeks in index and contact cases



The above scatter plot (Figure 40) details the differences in the constitutive melanin measurements before and after the monitoring period. The differences represented are modest and did not change significantly between visits, other than one subject in the contact group whose skin became darker. One would not expect to see large changes in constitutive melanin, as generally, these values reflect base-line melanin measurements prior to any tanning process. These measurements were taken from a body site not normally exposed to the sun. The change noted in case C1 is, therefore, an outlier and most probably the result of measurement error.

Figure 41: Distribution of constitutive melanin in index and contact cases before and after monitoring

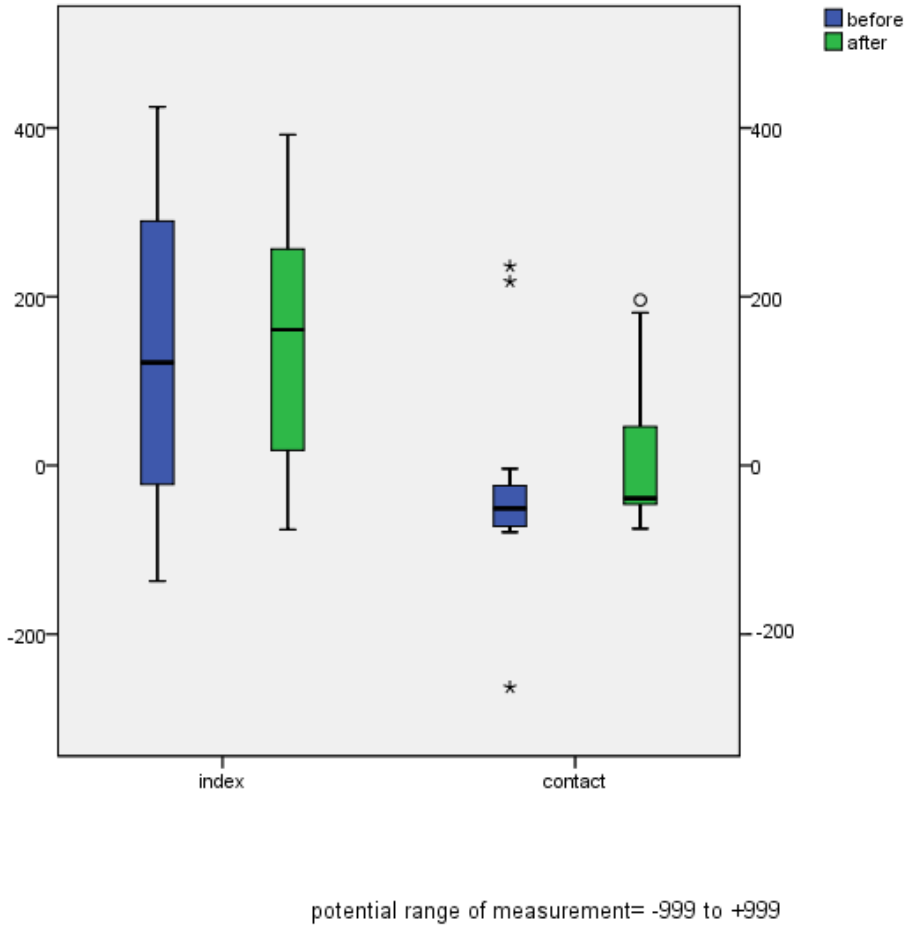


Figure 41 above shows that the index group had darker skin colour than the contact group and that there was very little change in skin colour in both groups following the monitoring period. These data provide a measurement of constitutive melanin, taken from a body site that is rarely exposed to sunlight. Although there were three outliers in the contact group, in general their skins were paler than the index group and the range of colour in the index cases more discreet.

Figure 42: Distribution of facultative melanin in subjects before and after monitoring

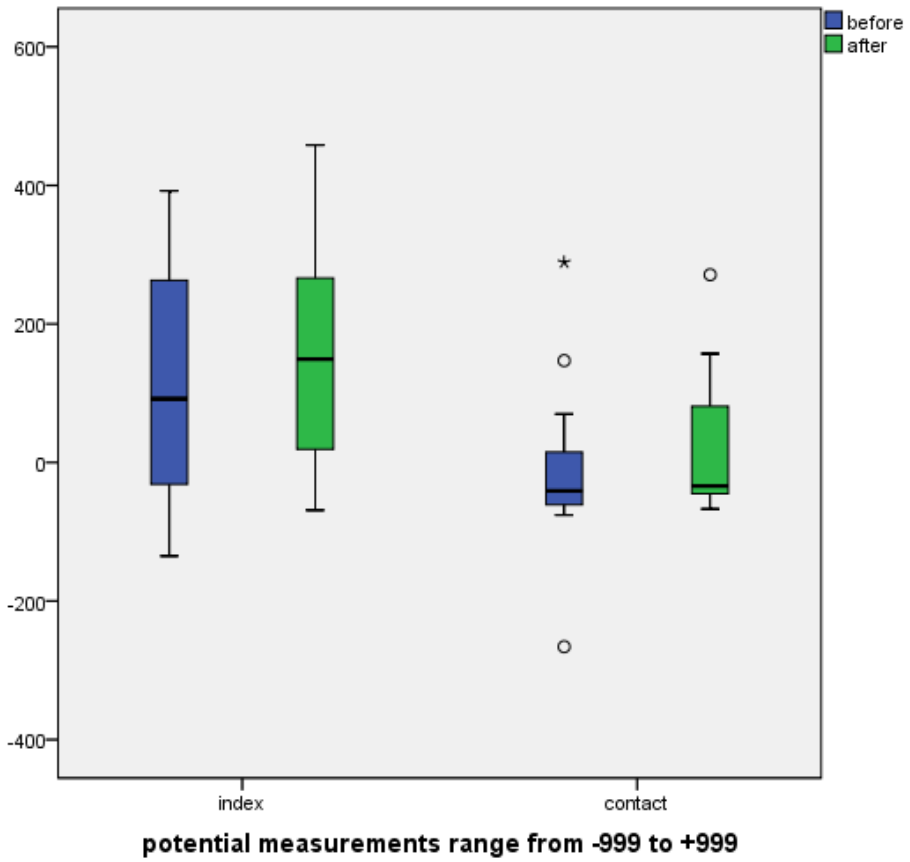


Figure 42 shows the distribution of the facultative melanin before and after the monitoring period in both groups. These show a minimal change in both groups. As the facultative melanin index changes as a result of tanning, and the site of measurement (dorsum of the hand) is a commonly exposed site, changes can be quite marked depending on the photo-reactivity of the skin and its ability to tan. The lack of tanning agrees with the very low sun exposure data obtained from the PS films in those whom returned them.

Figure 43: Changes in facial melanin density in index and contact cases

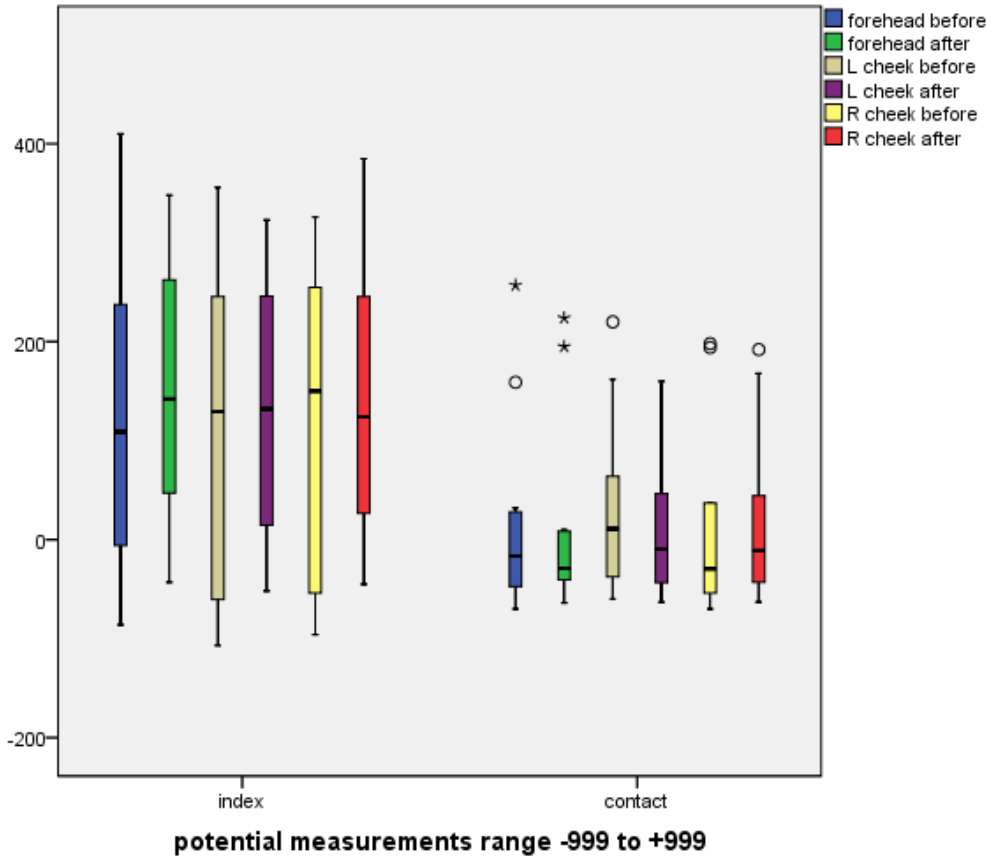


Figure 43 shows changes in melanisation over the monitoring period, broken down into the facial categories (facultative measurements) which are likely to display changes as a result of tanning. One can see that changes in the median and range of these data are minimal and demonstrate no evidence of tanning as a result of sun exposure in index cases. One can see that in the contact group (the paler group), very little change occurred during the monitoring period, which supports the low levels of sunlight exposure measured in the returned films. If any tanning did occur, it would perhaps be more marked in the paler group, as skin types 2/3 can appear very pale prior to tanning and become quite dark as a result of sunlight exposure whereas black skins, that have a high constitutive melanin content, would require high levels of erythemal UV to darken significantly.

7.10.6 How did skin type and colour relate to 25(OH)D levels?

Figure 44 and Figure 45 show that there is no significant relationship with Vitamin D status in the index group when plotted against the photo relative skin type categorisation of Fitzpatrick. Once can see that subjects with skin type 2 and above display 25(OH)D levels in the insufficient range other than the one outlier who was supplemented with Vitamin D. In the contact group the data points are more spread out with a stronger correlation suggested.

Figure 44: Relationship between 25(OH)D and Fitzpatrick skin types in index cases

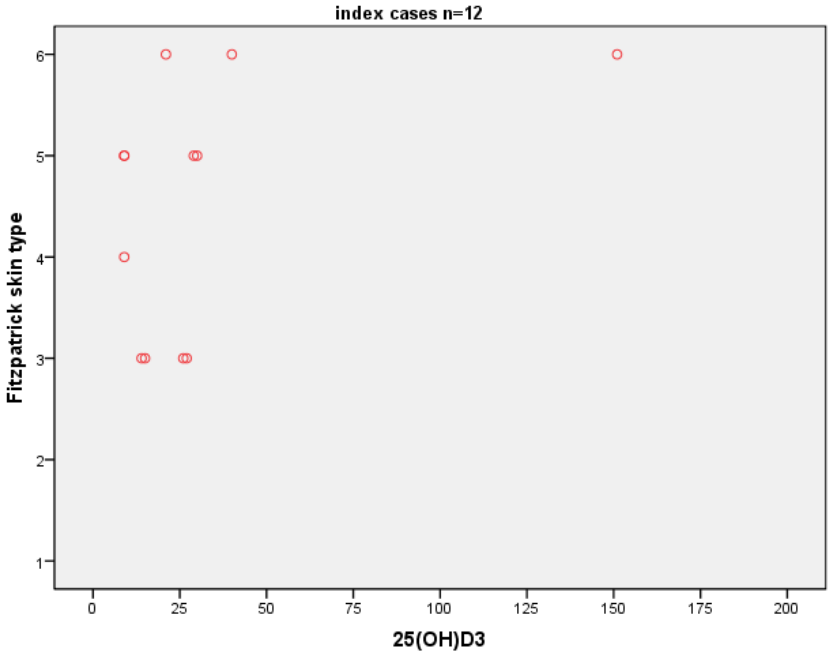
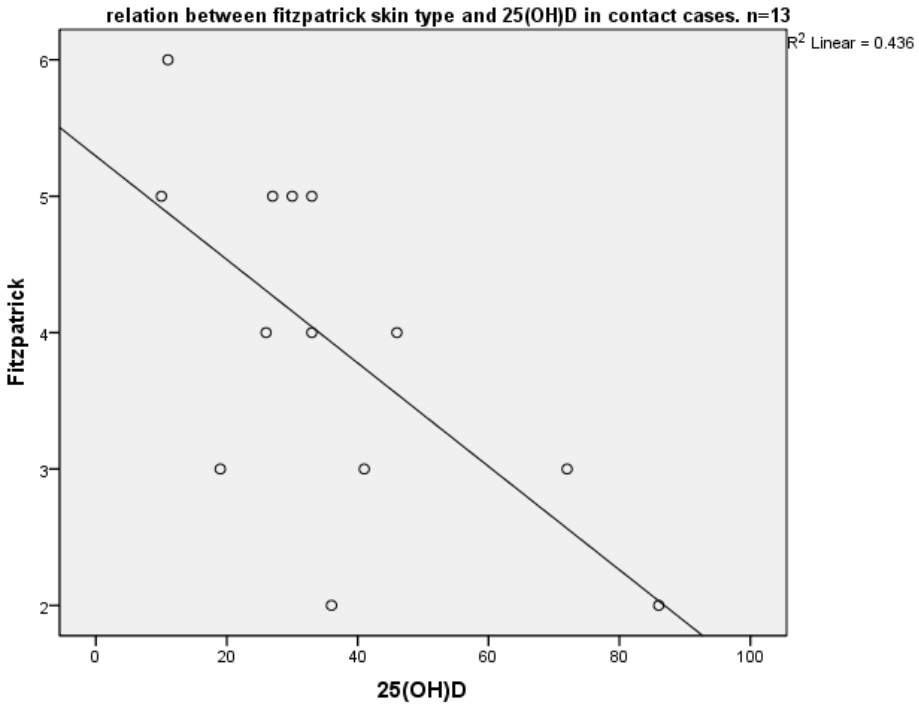


Figure 45: Relationship between 25(OH)D and Fitzpatrick skin type in contact cases



If we re-examine this relationship using the melanin index to measure skin colour rather than the self-reported scales, as shown in Figure 46, the result is not significantly different. However, it is perhaps more noticeable, that there are a number of cases with very pale skin that have Vitamin D levels within the deficient and insufficient range. In the scatter plot shown in Figure 47 we can see that, in the contact group, there is no significant change in the relationship between skin colour and Vitamin D, status but it is perhaps clearer to see that the group comprised of a greater range of skin colours and a broader range of Vitamin D results ranging from deficient to optimal.

Figure 46: Relationship between 25(OH)D and melanin index, in index cases

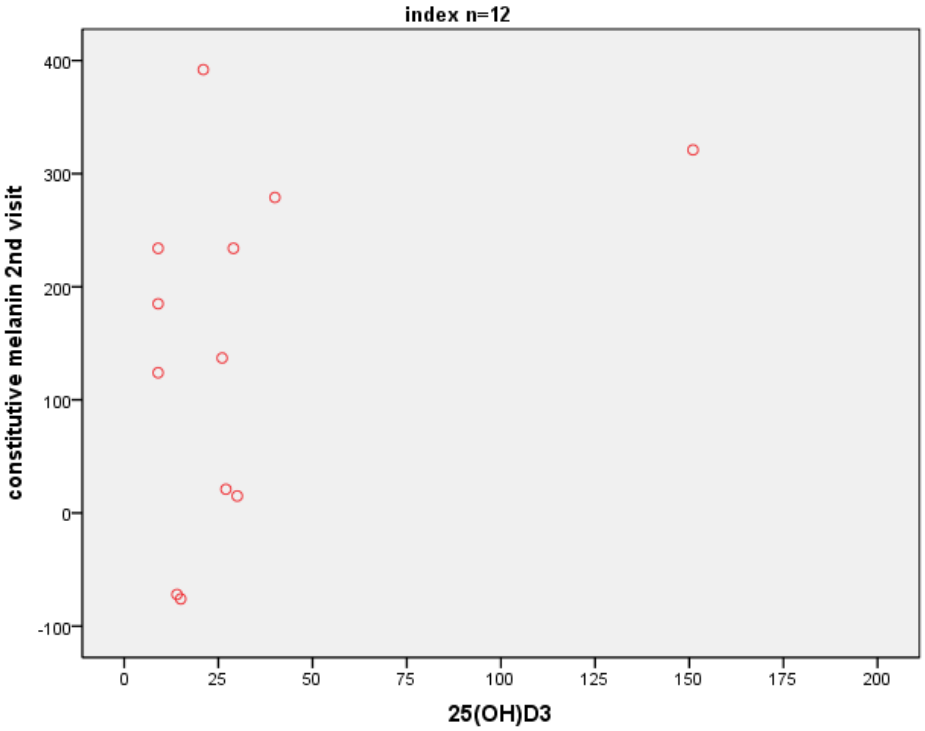
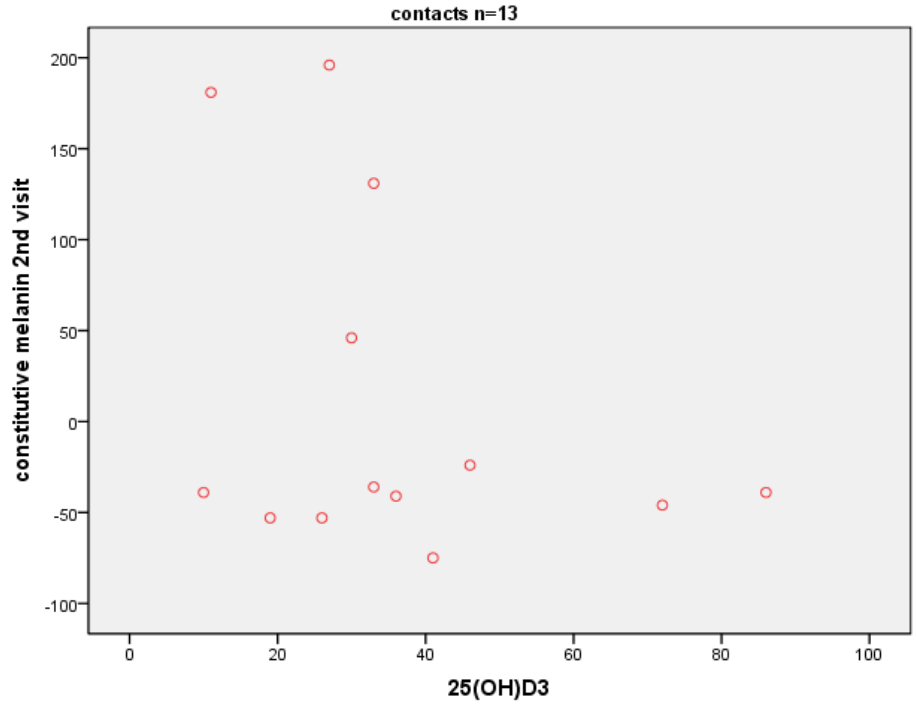


Figure 47: Relationship between 25(OH)D and melanin index in contact cases



These results suggest that there is no significant relationship between skin colour and Vitamin D status. This is in contrast to studies that have exposed subjects to measured UV doses and have shown that paleness of skin is positively associated with increasing Vitamin D status(227). However, the sample size of our study and the limited range of skin types did not allow any meaningful analysis.

7.10.7 Discussion and conclusion

Diffey's approximated measure of a Vitamin D producing dose, based upon Holick's rule, did not predict the Vitamin D status accurately in a significant proportion of either index or contacts cases in this study. I employed the method in this study in order to attempt to predict (approximately) the SED required to generate sufficient Vitamin D status in index and contact cases and compare them. The method only however, provides an estimate. Furthermore, the measured SED of the subjects who returned the films were very low and, in most cases, well below erythemal levels and the reported exposure proposed by this approach. Even those subjects with paler skins were deficient, or were unable to generate optimal levels of Vitamin D during the monitoring period. The skin colour measurements show that there was no significant tanning of the skin, which may indicate limited sun exposure which supports the low readings obtained by the films

Subjects in both index and contact groups displayed vitamin D deficiency and insufficiency. However, there were no significant differences between groups in the extent of deficiency noted, other than that patterns of these data varied (greater range in the contact group of both skin types and Vitamin D levels and a clustering of deficient and insufficient levels in very dark skins in the index group). These results conflict with a recent systematic review and meta-analysis which showed that on average, those with Tuberculosis have statistically significantly lower levels of Vitamin D than healthy controls(228) yet, the sample achieved in my study is too small to provide any powered results. However, more recent studies are beginning to report Vitamin D deficiency in the general population and, more specifically, a recent trial of TB supplementation found a significant proportion of contact cases with deficient and insufficient values(229). The systematic review was careful to include only those contact cases that were comparable to the index cases, yet their study and meta-analysis was derived from non UK populations as well as UK data. Notably,

one study undertaken in London showed some of the lowest levels of Vitamin D status in both index and contact groups(143). In both groups in the study reported here, it was possible to see that, regardless of season most subjects did not achieve a sufficient level in their Vitamin D status ,which also contradicts a seasonal pattern to Vitamin D status noted in both large population studies(230) and other smaller studies(231). Sunlight exposure and Vitamin D status were more closely correlated in the contact group than the index, although the contact group provided more films from which this could be calculated. The index group spent less time outdoors and this agreed with their SED measurements. This finding supports other workers who have noted Vitamin D deficiency in healthy controls, although reasons for this are not generally stated. It is possible that there is a 'city effect' and these low levels are a reflection of urban lifestyles. For instance, a study undertaken in Brisbane, Australia at the end of summer showed a surprising amount of Vitamin D deficiency and insufficiency in an otherwise hot and sunny climate(232).

Based upon these limited results, it is possible that Diffey's model may over estimate personal exposure dose or underestimate exposure dose and its relationship to cutaneous Vitamin D production. It is equally possible those subjects reported inaccurately and that the darker skins profoundly affected Vitamin D status although even pale skinned individuals showed Vitamin D deficiency. It may also be the case, that ambient levels vary according to atmospheric conditions and these variations may result in differences in potential ambient exposure. Additionally, most subjects reported minimal skin surface exposure when outdoors, with most subjects reporting only 6-10%, regardless of season. It has been suggested that skin area exposure could be more significant in the synthesis of vitamin D than time of exposure(231), and perhaps the model did not accurately account for this. It is important to note however, that the % SED only claims to provide an estimate of Vitamin D producing energy received and does not claim precision.

Studies undertaken where subjects were totally deprived of sunlight are useful in illustrating the extent of deficiency that occurs over time. One such study was conducted in a group of submariners who had their Vitamin D status measured before and after a 68 day period of sun deprivation. The mean serum levels fell from 78nmols/l to 48nmols/l over the study period(233). These men were essentially living

in the dark for the duration of the study. Estimates aside, the subjects who took part in our study, regardless of spending time outdoors exposed to the sun, were mostly unable to achieve the levels of the submariners who were completely deprived of light. The measurement period was also similar (2 months). It is very surprising to consider that living in the city maybe akin to living in darkness.

Conversely, when subjects are exposed to measured doses of UV, such as in Yesudian's study(234), one can appreciate the potential for rapid production of Vitamin D cutaneously. They exposed subjects to 3 measured doses of sub-erythemal UVB (70 mJ/cm^2) on three consecutive days, resulting in a doubling of serum $25(OH)D_3$ during the study period, in UK Asian subjects. However, this irradiance was given to 90% of the skin surface and this exposure is very unlikely to mirror casual exposure of most people living in cities but demonstrates the importance of skin exposure.

There is, of course, the very obvious limitation of sample size in the study reported here and as a result these data have been presented using a case study approach. There were two interesting 'signifiers' in the index and contact group subjects. Both cases were exposed to significant UVR, of a magnitude estimated to be above the dose required to synthesise Vitamin D to 'adequate' levels. Yet they showed lower exposures to other subjects who were able to generate more Vitamin D, when skin colour and % of skin exposed was taken into account. One contact had latent Tuberculosis and the other had active disease. It is, therefore possible that there is some validity in the argument that UVR exposure is not related to Vitamin D deficiency in those with Tuberculosis , which would support the findings of the Lumsden group(152), upon which this investigation builds. Then again, there are many other factors that could explain this anomaly. Personal UVR measurement is very complex and a number of assumptions are made that may lead to inaccuracies in estimating sunlight doses. Moreover, models do not take into account variations that occur as 'real' people move and live through the built environment. Sun exposure models, fail to acknowledge that usually, sun exposure is casual, and this may not be enough to generate sufficient Vitamin D for health. Models make assumptions because they are based upon static conditions generated from controlled experiments. For instance, usually they assume a horizontal supine exposure of the body to a clear

sky(190;218;235), conditions that do not reflect the exposure behaviours of city dwellers. The data obtained from my study support the view that 'real' people do not reflect well the assumptions applied by these mathematical models, and that this may be particularly pertinent for urban dwellers. Other studies measuring Vitamin D status conducted in city environments have shown similar results. A study in Manchester showed extensive and profound Vitamin D deficiency in young healthy active girls. Although sun exposure was not measured in these cases, it is likely that the environmental impact on UVR exposure potential, was significant to this result(236). Exposure conditions in towns and cities are more likely to be affected by shadow and shade from buildings and trees, resulting in complex and variable patterns of sunlight distribution across a moving body through the cityscape.

Finally, I was compelled to address the question of whether the average ambient levels of monthly UVR were representative of London measurements, given the city context and the micro- climate of the city that may act to attenuate UVR levels. It might have been the case that the ambient measurements taken at Chilton (a rural site) as a measure of the potential daily exposures were not representative of the UVR ambient levels in a city environment. This possibility will be explored later in the next chapter.

7.11 Question 3. What are the differences in dietary intake of Vitamin D between index cases and unaffected contacts and how does this relate to Vitamin D status?

Vitamin D_3 and Vitamin D_2 are found in small amounts in some foods. In order to determine whether dietary sources made a significant contribution to the Vitamin D status of the subjects, they were questioned, on inclusion into the study, about the frequency in which they consumed Vitamin D rich foods. The food frequency part of the questionnaire was developed by Martineau et al(126) for use in a recent Vitamin D supplementation trial of Tuberculosis patients and was adapted from the nationwide birth cohort study. This large population study included 7437, subjects from 1958 until the age of 45. These workers determined prevalence of Hypovitaminosis D in association with diet and other lifestyle factors(230).

7.11.1 Method

On the first study visit, and following consent, subjects were asked to report the frequency of intake of Vitamin D rich foods according to a ranked frequency scale. Categories included: never, occasionally, < once a week,1-2 times a week, 3-6 times a week, daily, 1-4 times a day or more than 4 times a day(230). Oily fish, the richest source of Vitamin D was described as mackerel, salmon and trout according to(126;230), but I also included tuna fish, marlin and sardines. These 'tropical' oily fish are eaten quite widely by many Mediterranean and African people. Frequency of ingestion of liver, eggs, margarine and cereals were also assessed. Martineau et al report that margarine in the UK is the only food where Vitamin D supplementation is added at 7.05-8.82μ g/100g, and this is a mandatory requirement(126). However, I was able to find brands with levels below this quoted amount with 5μ g/100g being quite common. Vitamin D supplementation of some cereals is also quite common (but not all). I was able to find Vitamin D in Cornflakes and Coco Pops at (1.7μ gs/100g), through my own investigation. I also assessed the use of Vitamin D supplements among the sample.

The scatter plots in Figure 48 and Figure 49 show the relationship between the frequency of ingestion of oily fish, such as salmon, mackerel, tuna, sardines and marlin with 25(OH)D status, in both index and contact groups. The y axis denotes the frequency of ingestion, with 1= the greatest frequency (more than 4 times a day) to 8=never. One can see that there is no significant correlation in either group. The range in frequency in the index group was from 1-2 times a week to never and the contact group ranged from 3-6 times per week to never. In order to achieve a daily dose of 400 IUs per day it is estimated that one would need to consume 25-100gs of oily fish per day such as sardines(237). Other varieties of oily fish are reported to contain lower levels of Vitamin D which would, therefore, require more frequent and larger portions of such fish as mackerel and salmon to achieve this dose(238). It is clear that neither group routinely ate enough fish to achieve this minimal intake and the quoted dose of 400IU per day is probably too low(239;240). The recommendations of such doses are, in fact not derived from scientific study but have been approximated from the contents of a teaspoon of cod liver oil, and its efficacy in the treatment of Rickets(241). A review by Heaney suggests that, in order to achieve

optimum levels, a daily dose of at least 2,000IU would be required(242;243). It is also likely that modern farming techniques affect the content of Vitamin D in fish such as salmon when compared to wild varieties, which are less frequently consumed.

Figure 48: Oily fish ingestion associated with 25(OH)D in the index group

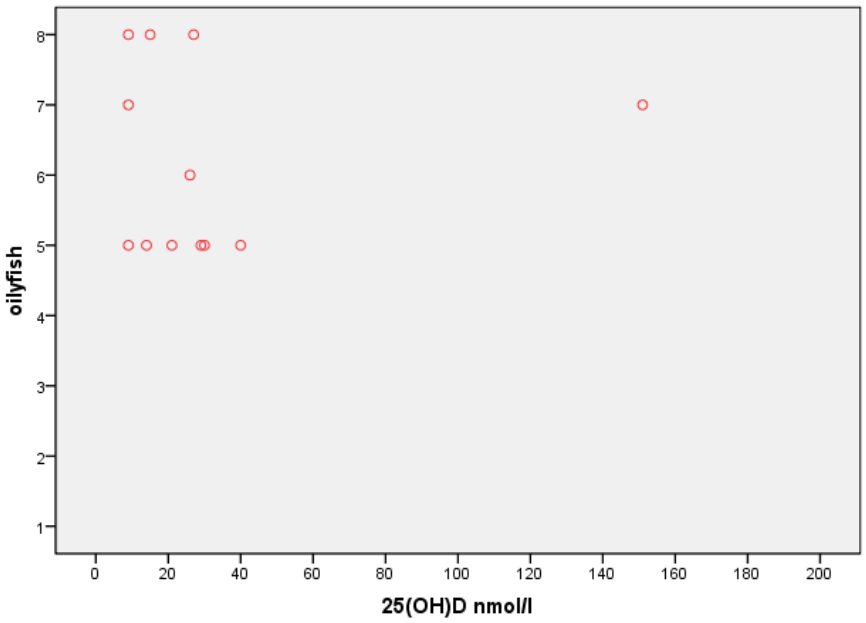


Figure 49: Oily fish ingestion associated with 25(OH)D in the contact group

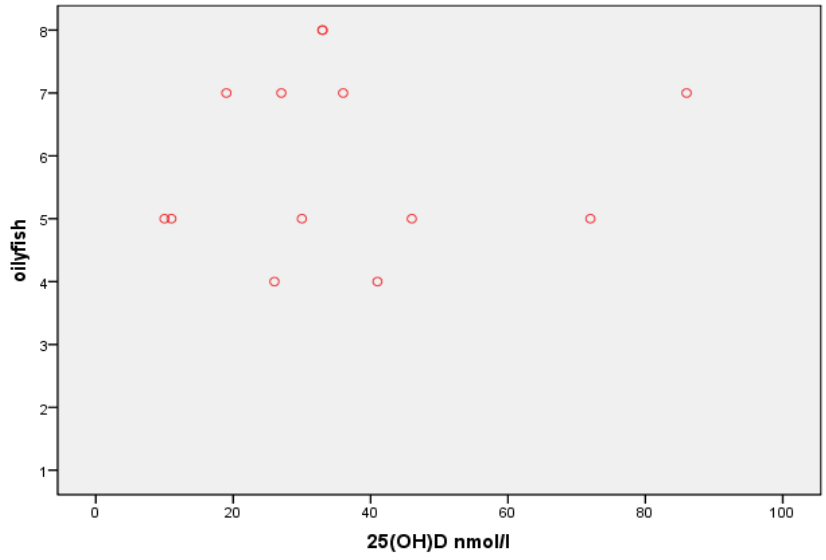


Figure 50: Margarine ingestion in index cases

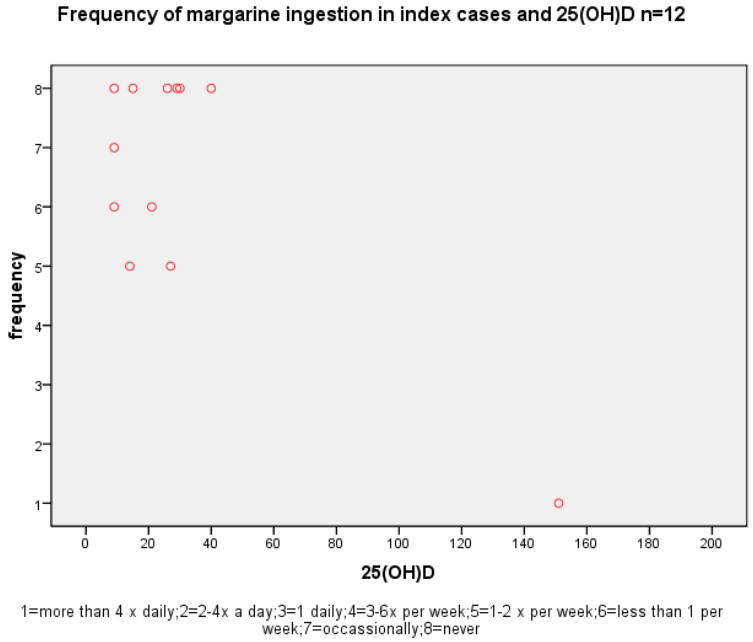


Figure 51: Margarine ingestion in contact cases

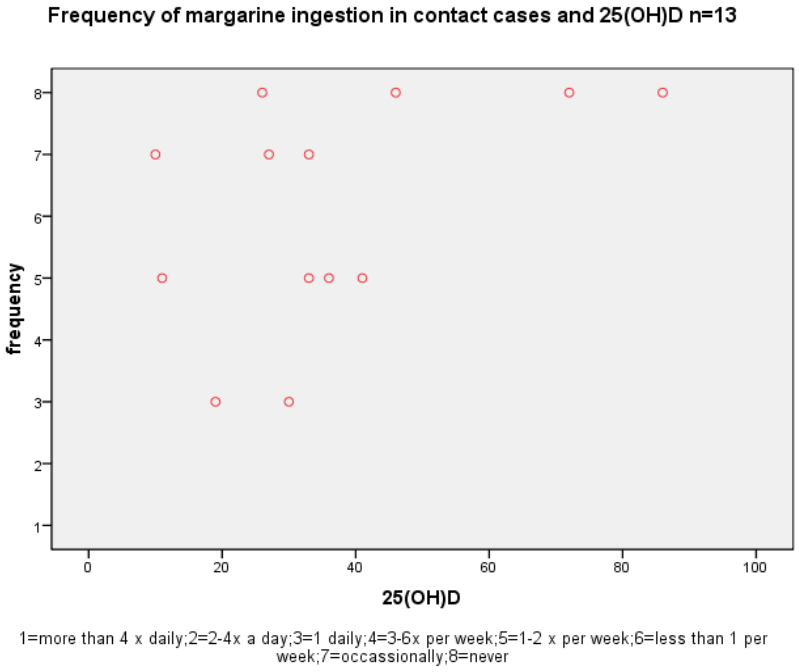


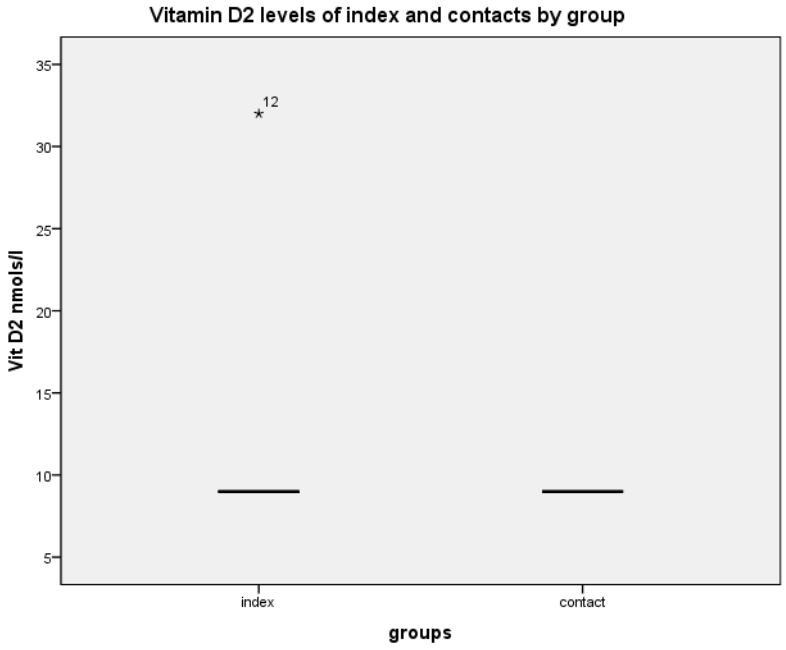
Figure 50 and Figure 51 show the frequency of margarine ingestion of both the groups. In both groups there is no relationship between the frequency of margarine ingestion and Vitamin D status. In the contact group those subjects with the highest

Vitamin D levels consumed margarine less frequently than those who showed deficient and insufficient levels. A similar pattern is shown in the index group.

7.11.2 Vitamin D_2

Figure 52 shows the Vitamin D_2 status of both groups. The assay is not sensitive to levels below 10nmols/l. In both contact and index groups all subjects, other than one in the index group (case 12), showed undetectable Vitamin D_2 levels. This suggests that probable intake of Vitamin D_2, through plant sources such as mushrooms and other plant matter, eggs and some fortified foods did not occur. The case that displays 32 nmol/l was taking a multivitamin supplement that could have contained Vitamin D_2 although the subject reported not taking the supplement for a month prior to the study and could not remember the brand of the supplement taken.

Figure 52: Vitamin D_2 status of index and contact cases

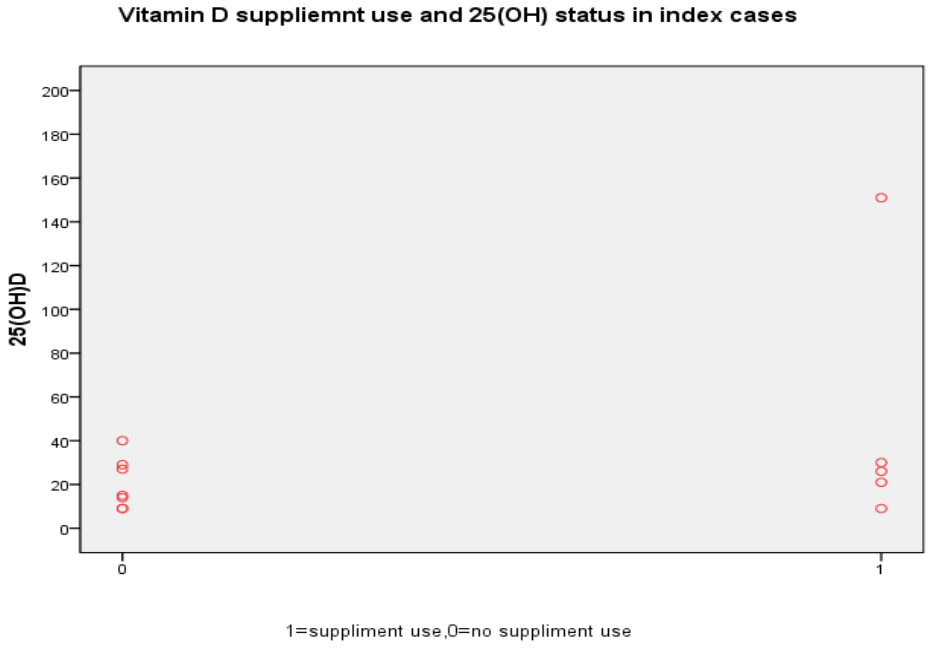


7.11.3 Supplementation

A number of subjects reported taking some form of supplement, usually over the counter preparations of multivitamins or cod liver oil. Seven Seas was the most frequently quoted supplement of those subjects who could remember the preparation. This product typically contains 400 IUs of Vitamin D_3. Figure 53 and Figure 54 show the frequency of supplement ingestion in both groups. In order to test the significance

of the relationships between the variables of supplementation and Vitamin D status, a non parametric test was selected due to the very small sample size. An independent samples Mann-Whitney U test was computed for both index and contact groups. The test summaries are shown with the scatter plots. In the index group there was no significant relationship between supplementation and Vitamin D status (sig=0.462, P= 0.05) but, in the contact group, this relationship was significant (sig=0.028, P=0.05). These results show that the contact group's vitamin D status was more strongly determined by supplement use than the index cases, regardless of the one clear outlier in the data and the equal use of supplements in both groups. It may be that the index cases did not report accurately their supplement use or it could suggest a difference in metabolism of Vitamin D in this group. Given the small sample, it would be unwise to infer any real significance to these findings.

Figure 53: Relationship between supplementation and 25(OH)D in index cases

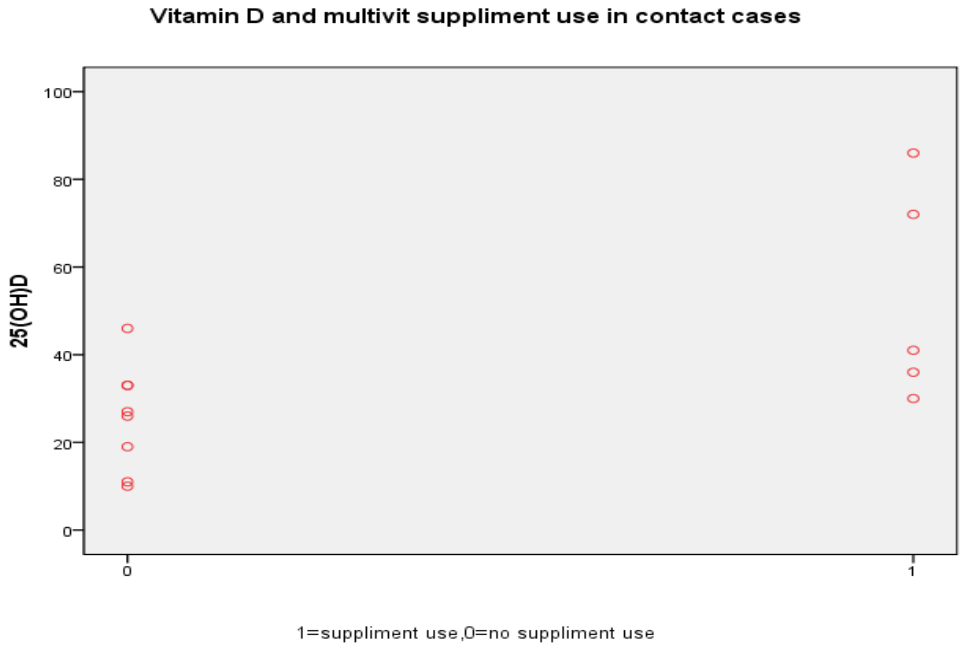


Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of postH25 is the same across categories of supplimentuse.	Independent-Samples Mann-Whitney U Test	.462	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 54: Relationship between supplementation use and 25(OH)D in contact cases



Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of postH25 is the same across categories of supplimentuse.	Independent-Samples Mann-Whitney U Test	.028	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

7.11.4 Other factors influencing Vitamin D production

As outlined at the beginning of this chapter there are a number of other personal behaviours that can influence the potential for Vitamin D sufficiency other than exposure to sunlight and levels gained from ingestion of foods containing Vitamin D. Sun bed use, sunscreen use and cosmetic use can also influence Vitamin D production, because many cosmetic products these days contain significant levels of sunscreen (which surprised many of the women who took part in this study). This can result in the inadvertent use of sunscreen on a daily basis to the face in particular and sometimes the hands. Use of such products may significantly reduce UVB reaching

the skin, especially if only the hands and face are exposed (6-10% of skin surface), the amount of skin exposure quoted as necessary for generation of Vitamin D. Most of the subjects reported only exposing this proportion of skin, regardless of season. When subjects reported consciously using a sunscreen, this was factored into the sun exposure model. However, incidental use was not. I was conscious that this might have been a significant factor in the ability of the model to correctly predict the Vitamin D status of the subjects. When the frequency of cosmetic use was assessed, it became evident that there may have been significant potential for Vitamin D production to be inhibited in this way, but this only occurred in one index case who used a face cream containing factor 20 SPF daily. The other subjects that were predicted to have received sufficient radiant exposure did not use any additional product containing sunscreen. Table 39 shows the frequency in which the subjects used moisturisers ranging from daily to sometimes to never. The products highlighted with an asterix are known to contain Sun Protection Factor (SPF). SPFs typically range from 15-20 in moisturisers and foundation. The literature provides conflicting accounts of the impact of sunscreen on Vitamin D synthesis in the skin. It has been claimed that SPF of 8 is sufficient to inhibit UVB reaching the skin and thus limiting the activation of 7-dehydrocholesterol(174;244). 50% of both index and contacts reported using make-up foundation sometimes (all women). Deliberate use of sunscreen (that may have been additional to daily use of other products containing an SPF) ranged from 91% in the index group who reported never using sunscreen, to 23% of contacts who always used a sunscreen. 50% of the index group reported using make up foundation sometimes, many of which contain a SPF. Unfortunately, not all subjects could remember the exact product they used but, where they were able to identify products, I have checked these, and those containing sunscreen are indicated in the tables. Typically, I found that certain cosmetic houses would include SPF in most moisturisers and make-up foundations, and these were usually at the high end of the market, as opposed to the cheaper brands which typically did not include sunscreen. Sunbathing is reported in the frequency of ‘active sun seeking’ and sun bed use over their lifetime and these are reported in the tables on the following pages.

Table 39: Tables showing frequency of sun-bed use, sunbathing and cosmetic use

Active sun seeker

Group			Frequency	Percent	Valid Percent	Cumulative Percent
index		Never	7	58.3	58.3	58.3
		Sometimes	5	41.7	41.7	100.0
		Total	12	100.0	100.0	
contact		Never	5	38.5	38.5	38.5
		Sometimes	8	61.5	61.5	100.0
		Total	13	100.0	100.0	

Sunscreen use

Group			Frequency	Percent	Valid Percent	Cumulative Percent
index		Never	11	91.7	91.7	91.7
		Occasional	1	8.3	8.3	100.0
		Total	12	100.0	100.0	
contact		Always	3	23.1	23.1	23.1
		Never	6	46.2	46.2	69.2
		Often	2	15.4	15.4	84.6
		Often whilst sunbathing	1	7.7	7.7	92.3
		Sometimes	1	7.7	7.7	100.0
		Total	13	100.0	100.0	
Sun bed use (lifetime)			Frequency	Percent	Valid Percent	Cumulative Percent
index		Never	10	83.3	83.3	83.3
		rarely	2	16.7	16.7	100.0
		Total	12	100.0	100.0	
contact		Never	13	100.0	100.0	100.0

Face cream use

Face cream : Group			Frequency	Percent	Valid Percent	Cumulative Percent
index		Daily	2	16.7	16.7	16.7
		Daily -baby lotion	1	8.3	8.3	25.0
		Daily- baby lotion	1	8.3	8.3	33.3
		Daily-palmers coconut cream	1	8.3	8.3	41.7
		Never	1	8.3	8.3	50.0
		No	2	16.7	16.7	66.7
		Occasional	1	8.3	8.3	75.0
		Occasional-Cocoa butter	1	8.3	8.3	83.3
		Occasional-E Arden body cream	1	8.3	8.3	91.7
		Occasional- Nivea for men	1	8.3	8.3	100.0
		Total	12	100.0	100.0	
contact		Daily -Garnier red*	1	7.7	7.7	7.7
		Daily -No 7 for men	1	7.7	7.7	15.4
		Daily -Vichy thermal S1	1	7.7	7.7	23.1
		Various	1	7.7	7.7	30.8
		Daily-Clinique*	1	7.7	7.7	38.5
		Daily-factor 15*	1	7.7	7.7	46.2
		Daily-No7 protect and perfect	1	7.7	7.7	53.8
		Never	5	38.5	38.5	92.3
		Occasional baby lotion	1	7.7	7.7	100.0
		Total	13	100.0	100.0	

Hand cream use

Group			Frequency	Percent	Valid Percent	Cumulative Percent
index		Daily	1	8.3	8.3	8.3
		Daily- baby lotion	1	8.3	8.3	16.7
		Daily-Palmers	1	8.3	8.3	25.0
		Never	5	41.7	41.7	66.7
		Occasional	2	16.7	16.7	83.3
		Occasional-Dove	1	8.3	8.3	91.7
		Occasional-Nivea	1	8.3	8.3	100.0
		Total	12	100.0	100.0	
contact		Daily	2	15.4	15.4	15.4
		Daily-astral	1	7.7	7.7	23.1
		Daily-Nivea	1	7.7	7.7	30.8
		Never	6	46.2	46.2	76.9
		Occasional	2	15.4	15.4	92.3
		Occasional-Dove	1	7.7	7.7	100.0
		Total	13	100.0	100.0	

Make-up foundation

Group			Frequency	Percent	Valid Percent	Cumulative Percent
index		Daily-Laura Mercer Factor 20*	1	8.3	8.3	8.3
		Never	6	50.0	50.0	58.3
		Occasional-Fashion Fare	1	8.3	8.3	66.7
		Occasional-Lancôme*	1	8.3	8.3	75.0
		Occasional-MAC*	1	8.3	8.3	83.3
		Sometimes	2	16.7	16.7	100.0
		Total	12	100.0	100.0	
contact		Daily in winter-Visible lift L'Oreal*	1	7.7	7.7	7.7
		Daily-Bobbi Brown*	1	7.7	7.7	15.4
		Daily-Dior SF 15*	1	7.7	7.7	23.1
		Never	7	53.8	53.8	76.9
		Occasional	1	7.7	7.7	84.6
		Occasional-Vichy	1	7.7	7.7	92.3
		Sometimes	1	7.7	7.7	100.0
			13	100.0	100.0	

7.11.5 Discussion

The inadvertent use of SPF in cosmetic products may have had a significant impact upon the ability of the female subjects, in particular, to synthesise Vitamin D in response to UV exposure, especially as most female subjects reported to 'sometimes' using products that contained SFP and also that most subjects did not expose their skin beyond 6-10% regardless of season. Unfortunately, this hypothesis cannot be confirmed or refuted by this study, due to the very limited sample. However, given the frequency of use and the wide prevalence of SPF in cosmetic creams and make-up, this variable would be essential to include in future work assessing the UV contribution to Vitamin D status in this population. Although the relationship between the use of sunscreens and its inhibiting effect on cutaneous synthesis of vitamin D is contested by some authors(174;245) it would seem likely that Holick's assertion of factor 8 inhibiting Vitamin D synthesis and factor 15 reducing capacity to produce Vitamin D by 98% is quite likely, if the products are properly and consistently applied . Given that many commercially available cosmetics contain sunscreen with factor 15 and 20 SPF, women should be made aware of the potential limiting effects this may have on Vitamin D production that could be achieved by causal sun exposure. Many of the subjects did not know that their products contained an SPF and were surprised by this fact. This is despite the very wide discussion and advertising in the beauty industry.

Inadvertent use of SFP may be particularly important for those women who have dark skins and are mostly covered, as in the case of Islamic women who wear a hijab and, therefore, only ever have the face and hands exposed. Moreover, it is becoming more common for Islamic women to adopt the full veil, and this may result in a significant health problem for these women living in city environments at relatively northern latitudes and intemperate climates.

Although these additional factors affecting Vitamin D status are interesting to investigate and would be important to quantify if I was able to achieve my recruitment target, it is difficult to determine their impact in such a small sample and to generalise these to the wider population. It is important to understand why this experiment was so difficult to achieve. I will now discuss the reasons why subjects declined to take

part in this study and the significance of these finding to the future of Tuberculosis research.

7.12 Why did subjects decline?

The reluctance to take part in this research, expressed by those who were approached was unexpected. This problem has not been reported in the literature before yet, it is not surprising, with hindsight, that there are so few studies that require such a commitment from Tuberculosis patients reported. It would seem that unless a treatment is offered to subjects, the burden of taking part in clinical research is too much to take on. The reasons provided for not wanting take part were varied but most significantly, many of these conformed to the idea of being stigmatised as a result of wearing the film. Many participants declined and gave reasons for not taking part at the point where an explanation was given regarding the requirement for wearing the film and I suspect that many of the reasons provided by subjects were in some cases excuses because they felt unable to say no. Being *'too busy'*, being *'too stressed' 'child care commitments, 'not wanting to give a reason'* and in some cases not being available to make further appointments, avoiding me in clinic and not returning messages showed a definite reluctance and unwillingness to be part of the experiment. It is very important to attempt to understand the reasons why people did not want to take part because the implication for future in-depth clinical science that involves this group will be extremely difficult to realise without it.

As already shown in Figure 28 on page 163, reported reasons for not wanting to take part in this study included: not wanting to be seen wearing the film; not having the time to come back to clinic; not wanting to be identified as 'different'. 8 patients were not approached at all, as it was thought that taking part would prove too burdensome for those already struggling to comply with treatment within a context of complex life problems. 4 young and trendy black men (contact cases) did not want to wear the film because it might impair their 'street image'. Other reasons why patients were unable to take part related to the work burden involved in the study, language and comprehension difficulties and personal stress related to the diagnosis that prevented a willingness to engage in the study. Some reasons provided were practical. For example, some were not staying in the area, preventing them from returning for follow-up visits, others reasons cited religious reasons, e.g., 2 index

cases who were screened, did not want to take part as the study would have taken place over Ramadan. Religious compliance prevented an initial meeting in one case (one subject would not shake my hand during Ramadan or allow me to touch him as I was female), which would have rendered the study procedures of blood taking and melanin measurement difficult. Drug and alcohol problems made some subjects unapproachable, as it was felt that extra work of clinical research would undermine their likelihood of compliance with treatment. In these cases I was guided by the opinion of the clinical nurse specialists, and I believed it was ethical practice to respect this view and not approach these individuals, and compromise their ability to comply with treatment. One patient was willing to take part in the study but would not wear the films, as he was anxious that the films would become the subject of scrutiny from the security staff at his station (Euro Star) i.e., he would be pressured into revealing his diagnosis. A number of subjects were needle phobic, which affected their enthusiasm to take part. Needle phobia also influenced my decision to approach some participants, 2 of whom had collapsed in clinic following Mantoux testing. The broad spectrum of reasons for declining this study were reported to the American Thoracic Society in May 2011 in Denver, Colorado, USA in the form of a poster presentation and published abstract(216).These results have been reproduced with permission of the American Thoracic Society. I continued to attempt to recruit patients into the study following submission of this paper to the ATS and have therefore, reported some reasons here that were not included in the original paper.

7.12.1 Conclusion

As a result of poor compliance with film use, reluctance to take part and the poor quality of some of the returned films, regardless of their successful application in other populations, regrettably I concluded that the use of Polysulphone film is not a reliable or acceptable method for personal UVR measurement in a TB population. With such a small sample achieving completion of the study, it would be presumptuous to conclude that this finding would maintain external validity in other TB groups, yet given the fairly typical demographic and the number of those who were asked to take part (a total of 126 index and contact cases combined), I feel confident that using the films would be troublesome in other TB groups as a method for quantifying personal UVR dose. As this is the first study that has employed their use in this population, I would advocate more research to seek either alternative

methods that are able to acquire the same level of precision as Polysulphone film, or explore the acceptability of other body sites where the dosimeter could be more acceptably placed. For example, the wrist has been found to be both reliable and acceptable in one other study(246), and this site may be perceived less obvious than the lapel. However, the issue of stigma is an important one, and in this study has been shown to be central to the motivation of Tuberculosis patients to take part in in-depth clinical research.

Unfortunately, I was unable to recruit enough subjects to test the study hypothesis however, in the sample that did agree to take part and wear the films; most subjects were not able to achieve sufficient Vitamin D status for health and these included healthy contacts. Additionally, many subjects who received radiant exposure deemed sufficient for healthy Vitamin D levels did not achieve these levels.

More work is needed to produce powered studies that describe UVR exposure accurately in the TB population to support or refute the contribution of sunlight to Vitamin D status in those with TB. Earlier in this thesis I reported the community perception of Tuberculosis in Brent where it was evident that Tuberculosis remains a stigmatised condition. It has not been reported before now, that the stigma of Tuberculosis limits and prevents engagement with clinical research. This is an important finding because it potentially influences the type of research that is possible in this group and potentially limits what it is possible to know and understand regarding risk factors for Tuberculosis beyond epidemiological descriptions. Any study that identifies a subject in any physical way, such as a film badge for example may be unacceptable for reasons of stigma. The requirement to wear a physical object for a clinical study *because* a subject has Tuberculosis has the potential to be further stigmatising. These sensitivities should be considered in the design and approach of method selection of studies in the future.

The failure to recruit to this work may also support another finding from the Brent study: that the identity of the researcher in the field is crucial to the success of clinical research and engagement of the community in which we seek to study. I was not an 'insider'; I did not have the subject's trust and may have been viewed more as an object of suspicion, than a health professional with an authentic interest in the individual. I did not have the advantage of being able to offer the subject anything

useful, such as a new treatment or intervention, which may positively influence decisions to take part in clinical research. It was more difficult to recruit index cases than contacts, but contacts dropped out more frequently and were less reliable.

The barriers to treatment discussed in the Brent study are transferable to the clinical research context where the ethnicity, gender and cultural history of the researcher is as important to the success of research as is the design and method. This is not normally a factor that is considered in quantitative study design because quite incorrectly, the researcher is conceptualised as an objective and impartial observer.

8 Chapter 8: UVR measurement in an urban environment. Does being in the city affect potential UVR exposures?

8.1 Introduction

In the previous chapter I followed a sample of TB patients over a period of 8 weeks, at different times of the year, in order to measure their UVR exposure and how this related to Vitamin D status. I was able to estimate the personal exposure dose through the use of methods described by other workers and total potential UV doses calculated from Chilton by the Radiological Protection Board. My results showed that Vitamin D deficiency and insufficiency was prevalent in both index and contact groups. Exposure doses, estimated as a the skin area exposure dose, based upon the frequently cited claim that sufficient Vitamin D will be generated under a certain set of conditions, did not provide accurate predictions of Vitamin D status in my sample. I have explored factors that might explain this finding, where it was possible to do so. One important factor that might vary depending upon location and local conditions is ambient UVR levels.

The quantity and intensity of UVR a person is exposed to, is a function of both exposure behaviour and potential ambient UVR. One important question remained outstanding and that was: does living in the city make a difference to the potential UV ambient exposure a person might receive? I was unable to find any published data of UVR levels for London, UK.

In this chapter I shall examine this question and compare data gathered from my experiments of UVR data gathered in Olympia, West London, with the more rural measurements obtained at Chilton. As well as the physical structures present in the built environment that may provide shadow and shade, the city can generate particular atmospheric challenges that act to reflect, attenuate, absorb and scatter UVR from a direct beam source (the sun). In particular, low level ozone, gases, aerosols and particulate matter from air pollution are common reflectors and absorbers of light(221;247;248).The mechanisms of absorption and scattering can profoundly affect the amount of available terrestrial UVR. These factors are briefly explored before I describe the methods and report the results of the London study.

8.2 Factors affecting UVR irradiance at the Earth's surface

We have noted that a number of factors influence how much UVR reaches the earth's surface, including the solar Zenith angle, cloud cover, absorption, ozone and albedo, that is, the reflective attenuation of light from various surfaces at ground level, such as snow, concrete and other reflective surfaces such as sand. Before UVR reaches the earth's surface UV rays pass through the earth's atmosphere and most of the high energy UVR is filtered out or absorbed (all UVC and most UVB). Increasing solar zenith angle extends the solar UV path length and also increases the amount of scattering by the atmosphere. It is estimated that only 6% of UVB, the biologically effective wavelength responsible for the synthesis of vitamin D, ever reaches the earth surface, yet it is responsible for 80% of biological effects both beneficial and detrimental(249). Some authors report terrestrial UVB to be less at 1%(248) others report 10%(248). The majority of high energy UVR is absorbed by Ozone in the stratosphere and scattered by molecules such as N_2 and O_2(249) Lower down, nearer the earth's surface in the troposphere, it is reported that ' absorption by pollutants such as ozone, NO_2 and SO_2 and scattering by particulates such as soot and clouds are the main attenuating processes'(249). The principal physical processes that define this phenomenon are the *Beer-Lambert law,* which describes the absorption properties of atmospheric materials in the path length of UVR from direct beam radiation(248) and *Raleigh* and *Mie* scattering, that describes the scattering potential of atmospheric particulates, air gasses and aerosols. I have previously described the effects of latitude and time of day on incident UVR, which are principally resultant from changes in solar zenith angle.

As ozone is the most affective absorber of UVR, it has been postulated that the generation of ozone and other particulate matter in polluted areas balances out the negative effects of ozone depletion higher up(250). It is further argued by other authors, that in the city, or highly polluted areas, the depletion of the ozone layer in the troposphere, which has been occurring for several years, allows more UVR to penetrate lower down, where it interacts with nitrogen dioxide and other products resulting in a *'photochemical smog'*(248). Although providing a paradoxical protective screen from increased high energy UVR, it is this photochemical smog that

results in the irritation of the epithelium of human lungs causing respiratory illnesses and ill effects reported as a result of air pollution in towns(248).

8.3 Measurement of potential UVR

In order to estimate personal UVR dose or SED one needs to determine the ambient levels of UVR that are potentially available. To my knowledge there is no published UVR data for London, with the nearest measuring station being in Chilton. Chilton, although near London, is quite rural and may not reflect the unique atmospheric conditions over London, to which the subjects in the previous study were exposed. Although the Chilton measurements for calculation of SED were used in the previous chapter, I wanted to be satisfied that these measurements were comparable to those in London given the variation in conditions that have been reported in towns.

8.3.1 Testing of Polysulphone film

The experiment that I am about to report uses Polysulphone film as a dosimeter to measure *daily* potential UVR. The previous chapters described a series of experiments that tested the film properties for use as a *personal* dosimeter. There were two considerations that I needed to explore to ensure that the measurements were as accurate as possible in this changed context. These included the tendency of the film to darken up to 24 hour after exposure and the potential for the films to continue to degrade *after this* time. Ie, did the films continue to darken after the 24 hour period? This would be important to determine as a) the films would not be read exactly after exposure or at 24 hours after exposure, therefore any continued degradation needed to be established. The literature only reports darkening up to 24 hours after exposure. And b), the selection of the most appropriate backing for the films to be mounted upon, given the variations in the reflective properties of different coloured materials. These two preliminary studies are now reported prior to the main experiment.

8.4 Does the colour of the background adhesive affect SED measurement?

Potential error may occur due to the reflective properties of the adhesive background selected to attach the films to the measuring station. It was important to ensure that the selected background (black Velcro adhesive) would not distort the results due to its absorbent or reflective properties. Previous research has demonstrated differences in the read outs of films when placed on contrasting backgrounds(251;252). These reports have noted that when Polysulphone film was placed on a background that was not 'flat black', then this increased the reading by up to 10%. Reasons for this increase are not explained in these reports. However, it could be the result of reflection through the film a second time from glossy or reflective surfaces behind the film. The object of the daily measurements in my study was to ascertain the potential ambient UVB exposure possible by month. In theory, a black backing would prevent reflection through the film a second time, once the light had passed through the film and made contact with the film backing. I decided to repeat a similar experiment to determine the most appropriate backing for the films to provide the most precise results.

8.4.1 Method

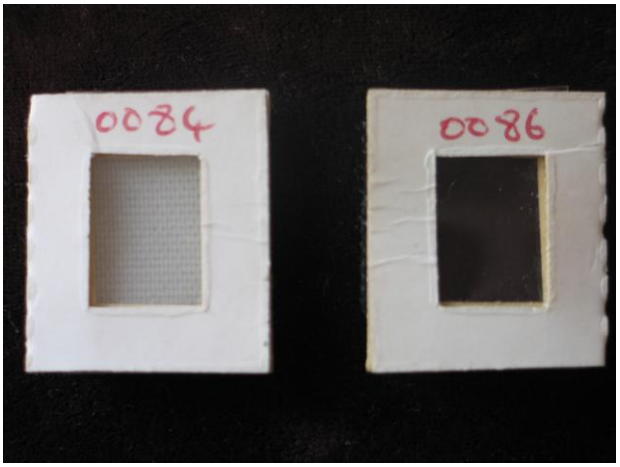
Two Polysulphone films were exposed for one day to midday direct sunlight upon a flat un-shadowed surface. One film was placed upon a white matt background and the other was placed upon a black matt background as shown in Figure 55. The films were read pre and post exposure in a spectrophotometer and the ΔA read at 330nm. The time of exposure was from 09.00 until 16.00 on a sunny cloudless day in July.

8.4.2 Results

The film placed on the black background recorded 43 SEDS for the day and the film placed on the white background recorded 40 SEDS. The high reflective surface of the white background appeared to make no significant difference to the measurement potential providing a reading 3 SEDS less than the black surface, a difference of 7%. These results contradict the findings of(251;252) who found the opposite effect, i.e. up to 10% difference associated with other backgrounds other than black). The pre

exposure status of the films in this pilot were comparable (0.1998, 0.1866 respectively).

Figure 55: Black and white adhesive background on films (not in situ)



8.4.3 Discussion

The unexpected 7 % reduction in reading from the black background could have been related to the high saturation of the film increasing the potential for error. Both films were at the saturation point where greater error is likely with reduced linearity in the relationship between exposure and degradation reported in the literature. Reports at what point the precision is lost vary enormously, with some studies showing increasing error at 0.9 and others reporting loss of linearity at much lower levels (0.3)(253). The potential for the film to saturate is a function of film thickness and the photoproducts produced by the degradation of the polymer (179;254). The films used in my study and in the personal monitoring in the previous section were 40μm and these were tested in the methods chapter at the beginning of this thesis. They appeared to remain stable up until 0.9. It is interesting to note that the daily reading on the measuring station was 70 SEDS (black background used at measuring station) when compared with 40 and 43 SEDS at very similar positions. Additionally the 'station' film was not removed until later in the day and, therefore, its potential to degrade continued until sunset when it was finally removed, whereas the experimental films, (used in the colour background experiments) were removed at 16.00.

8.4.4 Conclusion

I selected the black background for the daily measurements regardless of the unexpected result in this pilot experiment. Mt reason for this was that since a variation of 10% was reported for surfaces that were not flat black and my pilot study demonstrated a similar effect for the white film backing, it seemed that either way, regardless of which film backing I selected, a variation may occur. However, there was less potential for flat black surfaces to be reflective and therefore I opted for the black backing, throughout the period of UVR measurement, to ensure consistency.

8.5 Did the time of reading the film after exposure affect the measurement: Was there a 'dark' effect?

Another challenge in relation to Polysulphone film as a dosimeter is that it is subject to continued degradation following the exposure period, and this may affect the optimum timing when the films are read, in order to achieve the most accurate measurement. This dark effect is noted to occur up to 24 hours following exposure. As I was unable to get to the laboratory every day to read the exposed film directly following exposure (the films were removed at night), the films were taken to the lab in batches at varying times following their exposure. All films were read after this 24 hour period, when the darkening effect is reported and moreover, were read at different times following initial exposure, ranging from a week to a month afterwards. The literature reports a darkening effect in the film of about 4% following exposure(179). Given the variation in delay before the films were read, it was necessary to determine whether significant darkening of the film occurred *after* the reported 24 hour period, to ensure stability over time. One would also have to accept that a 4% variance may occur in the post exposure measurements of the film, as reported by other workers, although unfortunately, I did not test this.

8.5.1 Method

10 previously exposed films were re-read in a spectrophotometer. All films had been randomly selected from a batch of previously exposed films from which measurements post exposure had already been determined well after 24 hours. The first and the second readings were compared in order to determine any additional darkening effect.

8.5.2 Results

Table 40: Degree of 'dark effect' following exposure

First reading	Second reading	Variation
0.429	0.442	.013
0.429	0.437	.008
0.495	0.480	.015
0.336	0.326	.010
0.418	0.417	.001
0.420	0.409	.011
0.421	0.412	.009
0.413	0.400	.013
0.528	0.521	.007
0.376	0.370	.006

Table 41: Total Variance

Descriptive Statistics

	N	Mean	Std. Deviation	Variance
	Statistic	Std. Error	Statistic	Statistic
first	10	.01702	.05383	.003
second	10	.01715	.05425	.003
n	10			

Table 40 and Table 41 show the differences and variations between the first and second measurements and the total variation in these data. One can see that the variations in these measurements were very small, and thus I concluded that the reported dark effect would not affect the precision of the measurements significantly.

8.5.3 Conclusion

I concluded that the films remained stable in terms of their tendency to continue to degrade and that this property did not continue after the 24 hour period.

8.6 UVR measurements for London

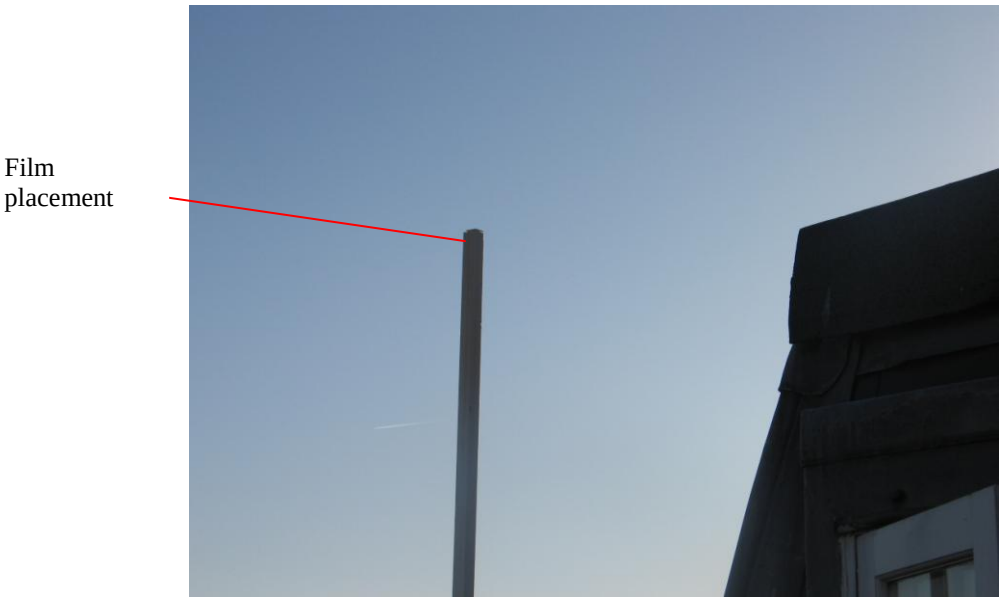
Following the pilot experiments that explored the possibilities for measurement error of the Polysulphone film, I planned my experiment. The following section reports the method and the results of the London UVR measurements. This study required that each day, I placed a film and at the end of the day, I personally removed it for the period of one year. On occasions, weather conditions prevented me from achieving a daily measurement and other variations in conditions of either weather or film properties resulted in some uncertainty regarding the quality of some of the measurements and these shall be discussed later on this section.

8.6.1 Method

Over a period of one year I placed Polysulphone film badges on top of a wood construction (Figure 56) that was fixed to a roof (**Error! Reference source not found.**) above any shadowing from other structures in Olympia, west London. The badges were adhered to the wooden stick using a Velcro black background (below photograph shows white background for illustrative purposes only) and changed daily or every other day in the winter months, to avoid saturation of the film. The films were read pre and post exposure in a spectrophotometer at 330nm, as previously described, and the change in absorbance (ΔA) calculated to reflect the potential daily UVR measurement for that day.

Figure 56: Polysulphone film adhered to measuring station

Figure 57: Measuring station in situ above the height of roof and adjacent shadowing



8.7 Results

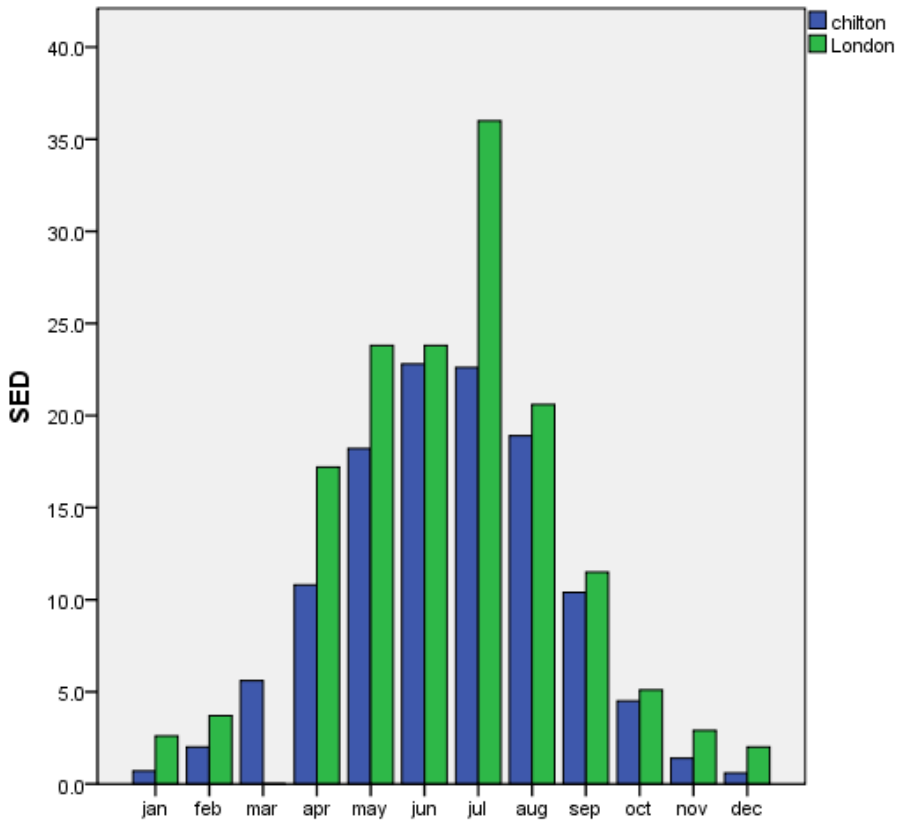
Table 42: Mean SED by month London UK from August 2009-July 2010

	N	Range	Minimum	Maximum	Mean	Std. Deviation
AUG09	31	62.10	3.50	65.60	20.6452	13.93956
SEP09	30	20.20	2.50	22.70	11.5467	4.44295
OCT09	31	11.40	.00	11.40	5.1871	2.98348
NOV09	30	6.40	.10	6.50	2.9933	1.24622
DEC09	31	3.40	1.00	4.40	2.0032	.75520
JAN10	31	2.30	1.80	4.10	2.6129	.59874
FEB10	21	5.40	1.80	7.20	3.7190	1.53415
APRIL10	30	17.80	7.70	25.50	17.2633	5.00954
MAY10	31	77.30	6.20	83.50	23.8710	18.26938
JUNE10	31	77.30	6.20	83.50	23.8710	18.26938
JULY10	28	110.30	2.70	113.00	36.1964	26.43329

Table 42 above shows the range, mean and standard deviation of the measurements obtained over the monitoring period, plus the number of days where monitoring took place. One can see that the highest SED of 36 is obtained for July, followed by May and June measurements. The lowest SED measurements were obtained in November, December, January and February. Figure 58 compares these data with the Chilton data. On the whole these data compare well. However, the London measurements are

of slightly higher for London for most months and much higher for the month of July. Unfortunately, data for March is missing as the source data was misplaced on public transport, returning from the laboratory and was not recovered.

Figure 58: Comparison of mean SED from London and Chilton (City and rural measurements)



A Pearson's correlation co-efficient was computed in order to determine the strength of the relationship between the data sets from the two sites. There was a strong correlation between the two data sets: r= .958, n=12, p= 0.01.

8.8 Measurement consistency

At times it was not always possible to obtain a measurement for a particular day, for various reasons. **Error! Not a valid bookmark self-reference.** outlines the days during the monitoring year where there were missing measurements and the reasons. I also included what actions were taken to mitigate the missing measurements. For example, where a film was left out for two days, as there was not an opportunity to change the film, the nearest legitimate reading was taken as a surrogate measurement for that day. Other sources of error included the adhesive film backing adhering

strongly to the Polysulphone, making its removal difficult, and subsequent damage or kinking of the film. This may have affected the read out of the film, as reported earlier in this thesis. In total, 43 days in the year were affected by such measurement errors, of which I am confident that the solutions provided would not have significantly affected the quality of the overall data.

Table 43: Measurement errors and number of days affected

Date	Nature of measurement problem	Corrective action	Number of measuring days affected
17/08/2009	Missing film	Last legitimate reading taken	1
29/08/2009	One film left out for 2 days (not saturated)	Last legitimate reading taken	2
10/10/2009	Removed film from station then left outside by mistake (not saturated)	Last legitimate reading taken	2
18/10/2009	Film left out for two days (not saturated)	Last legitimate reading taken	2
08/11/2009	Film casing opened during exposure affecting the position of the film to the sky (vertical not horizontal)	Last legitimate reading taken	1
18 / 09/2010	Severe storms and gale force winds forced removal of measuring station from the roof for 3 days	Last legitimate readings taken	3
21-27/11/2010	Away-no readings taken	Next legitimate readings taken and substituted for missing days	7
23/02/2010-21/03/2010	Missing data	No readings available	22
02/04/2010	Film adhered to adhesive backing causing kinking and adhesive deposits on the film which may have affected the readout	Last legitimate reading taken	1
07/6/2010	Missing reading	Last legitimate reading taken	1
16/06/2010	Missing reading	Last legitimate reading taken	1

8.9 Discussion and conclusion:

Although the London data showed slightly higher potential SEDs per month than the Chilton data; the overall agreement was relatively good. The slightly higher readings obtained in London may have been a result of the 'dark effect' of the film, that may have occurred within the 24 hours following exposure. This similarity in the data suggests that the potential for total ambient UV exposure in a large industrial city does not vary greatly from a rural site nearby. This is important, because it excludes local atmospheric conditions as a possible explanation for the Vitamin D deficiency in the sample.

There were, of course, differences in the method of measurement between the two compared datasets and the time over which the measurements were taken. The Chilton data represents averages between the period of 1991-2002 and the London data were taken from 2009-2010. Changes in weather alone can result in marked variation of terrestrial UVR. However, the comparison of these data assumes that the variations are similar from season to season and year to year. I acknowledge that this may not be the case, yet the fact that the London data agreed with the Chilton data gave me confidence that the variations did not differ greatly. Importantly, the similarity of these data provided assurance that the Chilton measurements could be used as an average data set for the UVR calculations without concern that they did not reflect average UVR in an urban setting.

This study shows that the potential for UVR exposure in a city is similar to that of more rural settings in the UK, regardless of reports in the literature that suggest reduced UVR at terrestrial levels in cities as a result of pollution and ozone. This study did not measure atmospheric conditions known to attenuate UVR, rendering any attribution of atmospheric affects unwise to these data. At best, my results show that the potential for sun exposure in the city is similar to that of the suburban environment. It is more likely that personal UVR exposure is more strongly influenced by exposure behaviour and time spent outdoors. London is still reported to be one of the worst offenders of air pollution in Europe, so it is unlikely that there was a sudden improvement in air quality over the time that my study took place.

Since ambient levels did not fully explain Vitamin D deficiency in either index or contact groups, there are two possibilities that could explain it, other than diet and sunscreen use. One is that the subjects did not accurately report other factors that are important to Vitamin D status. Secondly, if we assume that the SED measurements were accurate and that patients complied with the film wearing, then neither group was exposed to enough sunlight to ensure adequate D Vitamin levels. The contact group showed 25(OH)D levels that correlated more strongly with sunlight exposure than those of the index group. This raises the interesting possibility that supports the conclusion from the Lumsden group: that sun exposure is not the cause of Vitamin D deficiency in Tuberculosis patients, and that there could be some variation in metabolism i.e. a down regulation of Vitamin D occurring in these subjects. More research is required that can report powered studies that measure the relationship between UVR exposure at the individual level to refute or support its contribution. Unfortunately, I was unable to achieve such a study, as the use of Polysulphone film proved to be an unacceptable and unreliable method in most cases.

The very low readings obtained from the films that were returned by the subjects describes well an important element of urban life; that movement through the built environment and city lifestyles can prevent adequate exposure to UVR for Vitamin D synthesis. I have demonstrated that this is not a result of a lack of available UVB, but is more related to the personal exposure possible when people are 'out and about' in towns and cities. It would be useful to conduct studies in the general population to see whether these very low exposure rates are more generally evident, and whether the Vitamin D deficiency that was demonstrated in the contact cases of this study is typical of the wider population in London. This work supports that of other workers that have shown similar low levels of Vitamin D status in 'healthy' urban dwellers in France and the UK(236;255). Public health strategy should be directed towards providing solutions to Vitamin D deficiency in city dwellers in particular, as it would appear that the risk of such deficiency is greater in towns and cities.

8.10 What this thesis adds

Overall, this thesis has demonstrated why Tuberculosis research is difficult and has provided in depth insight into the lives of those who are at high risk of developing the disease that has not been previously reported in such a large sample. Additionally, I have explored how city life influences the Tuberculosis story in some profound ways, including the political context of migrant life, as was demonstrated in the community and health professionals' stories of treating immigrant and refugee groups. I have described the importance of sunlight in the Tuberculosis story, and how city living can mediate exposure to sunlight. To my knowledge, this is the first study that has measured UVR exposure in a cohort of Tuberculosis patients and comparable contacts. My results show that the city dwellers who participated in the study did not spend enough time in the sun to generate sufficient Vitamin D for health and, in most cases, did not achieve levels equivalent to submariners who were totally deprived of sunlight. The subjects also did not ingest sufficient sources of Vitamin D through their diets to compensate for their 'dark' living styles. It is difficult to say whether this is reflected more widely in the general population, but unless the diet is particularly rich in fish, then it is unlikely to be a significant source of Vitamin D. A simple solution would be to encourage greater sunlight exposure, as some experts have advocated(256;257), but this approach remains controversial and probably not advisable(218;258). Moreover, differences in metabolism have been observed between ingested Vitamin D and that obtained from sun exposure and these may be biologically important(257). Therefore, further research is needed to explore this point before 'safe' sun exposure is dismissed entirely.

Additionally, if one were to support the argument for increased safe sun exposure, it would need to be tailored to variations that are likely to occur as a result of season, skin type and latitude, as one size clearly does not fit all(259). Vitamin D synthesis in the skin is not exponential, as prolonged sun exposure causes a degradation of the excess compound to inactive metabolites, rendering UVR exposure beyond erythemal limits more risky than beneficial(140). The current consensus is that supplementation should be encouraged to correct low levels of Vitamin D in the body, although debate about sufficient dosage and optimum therapeutic levels remain the subject of much discussion and research(154;214;245;260).

The seasonal fluctuation in Vitamin D levels noted in other studies was not evident in the small sample who took part in this research, in contacts or index cases. This finding suggests that sunlight was not particularly important in determining their Vitamin D status but, in larger studies, this variation is clearly evident. It is interesting to consider, the evolutionary development of an endocrine system (Vitamin D synthesis and regulation), that has adapted to generate Vitamin D through cutaneous synthesis and the seasonal fluctuation that naturally occur in people of pale skins, living in the Northern hemisphere. One wonders whether the change in levels between seasons is biologically necessary. Can we be certain that advocating all year round Vitamin D levels within the optimal range is beneficial to health in the long term? Answers to questions regarding dosage, the best method of obtaining healthy levels and health benefits of optimal vitamin D status are remarkably difficult to unravel from assessment of the current and vast literature on this subject; as the authors tend to argue the case according to their own bias(261) .

In conclusion, this thesis has reported the following:

- There remains a significant stigma attached to Tuberculosis and this is complicated by the political and social context of urban life. Refugee and immigrant groups, for example, may be more vulnerable to the affects of stigma than indigenous groups, as a result of fear of exclusion and the requirement for social support as fundamental to survival and success in society, family life and migrant settling. This thesis has presented the first extensive qualitative study of social and attitudinal factors regarding Tuberculosis in Brent, London, UK and is among only two such studies in London. This thesis also reports for the first time, the consequence of stigma to participant engagement in clinical research. For clinical research into Tuberculosis this is an important finding as many scientists may overlook stigma as a factor that influences method selection for clinical studies. The use of visual instruments, for example, such as the polysulphone film badge, may represent to the participant a signifier of disease and this in itself can be stigmatising. This becomes extremely problematic when such visual signs are employed in the study of an already stigmatised condition such as Tuberculosis.
- The Brent study shows that the complexities of migrant life, stigma and fear of exclusion hinder engagement between health professionals and migrant/refugee

groups which affect case identification and treatment compliance, and the necessary relationships that are required between health professionals and those needing treatment.

- Factors often attributed to 'culture' may be common across groups, and health professionals should exercise caution when conceptualising the contribution of culture to human behavior as requiring a unique or special response in health care provision.
- People who are affected by Tuberculosis in cities live challenging lives and engagement in clinical research is difficult for them. This affects the possibility of future in-depth studies and is of great concern, if knowledge is to move beyond epidemiology, and obtain insights into causative factors that contribute to Tuberculosis risk that involve measurement at the individual level.
- This thesis presents the first study of personal UVR monitoring in a Tuberculosis cohort. These results show that Vitamin D synthesis is potentially impaired in city dwellers due to 'dark' living styles, and this is probably not exclusive to Tuberculosis patients. Those in cities may be at greater risk of Vitamin D deficiency, and this may contribute to the increased risk of developing disease as a result of the known immunological benefits of Vitamin D sufficiency. However, the relationship between sunlight exposure and Vitamin D status appears to be different in those with active disease than it does in healthy controls, suggesting that the direction of the relationship may be more strongly associated with Tuberculosis than it is with sunlight exposure. Larger powered studies are required to test this hypothesis.
- Polysulphone film is not an acceptable method in a Tuberculosis population for measuring personal UVR exposure, regardless of many reports in the literature that have found them acceptable in a range of populations. It remains important that UVR exposure and the relationship to Vitamin D status is explored further in this group and in different settings. An alternative method of measurement should be investigated. Controlled comparative studies of UVR exposure in a Tuberculosis group would be useful.
- Finally, the last study reported UVR data for London. These data show that the potential UVR exposure in an urban setting is not significantly different to a more rural setting however, factors such as the built environment and lifestyle may

uniquely affect city dwellers in the acquisition of sufficient radiant energy for the synthesis of sufficient Vitamin D status for health.

Tuberculosis remains a distressing and sometimes fatal condition. It is often considered a disease of the past and thrives best in conditions present in cities. Modern life has reinvigorated an ancient malady, regardless of progress, advances in medicine and science. Greater understanding is needed regarding environmental factors and the human relationship with the environment, in order that risk factors for disease can be avoided, given that a 'cure' for Tuberculosis has been in existence for some years. Further energy should be geared towards prevention, the development of effective vaccines, and improvement in living conditions, managing the health of migrant groups and the interplay of these factors and the influence of life style in general.

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APPENDIX

1 Appendix 1: Search Strategy Brent Study

No.	Database	Search term	Hits
1	CINAHL	exp TUBERCULOSIS/	7543
2	CINAHL	TB.ti,ab	2756
3	CINAHL	Tuberculosis.ti,ab	5184
4	CINAHL	1 OR 2 OR 3	8720
5	CINAHL	REFUGEES/	2503
6	CINAHL	(asylum AND seek*).ti,ab	439
7	CINAHL	refugee.ti,ab	820
8	CINAHL	exp HOMELESS PERSONS/	2149
9	CINAHL	homeless*.ti,ab	3130
10	CINAHL	5 OR 6 OR 7 OR 8 OR 9	6545
11	CINAHL	4 AND 10	220
12	CINAHL	exp ATTITUDE TO HEALTH/	53184
13	CINAHL	perception.ti,ab	15559
14	CINAHL	ANTHROPOLOGY, CULTURAL/	997
15	CINAHL	(social AND meaning).ti,ab	1779
16	CINAHL	exp CULTURE/	70126
17	CINAHL	COMMUNICATION BARRIERS/	2360
18	CINAHL	barriers.ti,ab	17497
19	CINAHL	knowledge.ti,ab	61129
20	CINAHL	12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19	195906
21	CINAHL	11 AND 20	54
22	CINAHL	LONDON/	0
23	CINAHL	london.ti,ab	4379
24	CINAHL	22 OR 23	4379
25	CINAHL	21 AND 24	3
26	CINAHL	4 AND 24	31
27	CINAHL	20 AND 26	8
28	MEDLINE	exp TUBERCULOSIS/	138621
29	MEDLINE	TB.ti,ab	19164
30	MEDLINE	Tuberculosis.ti,ab	120259
31	MEDLINE	28 OR 29 OR 30	174986
32	MEDLINE	REFUGEES/	5814
33	MEDLINE	(asylum AND seek*).ti,ab	727
34	MEDLINE	refugee.ti,ab	2545
35	MEDLINE	exp HOMELESS PERSONS/	5342
36	MEDLINE	homeless*.ti,ab	5286
37	MEDLINE	32 OR 33 OR 34 OR 35 OR 36	13504
38	MEDLINE	31 AND 37	937
39	MEDLINE	exp ATTITUDE TO HEALTH/	239095
40	MEDLINE	perception.ti,ab	76035
41	MEDLINE	ANTHROPOLOGY, CULTURAL/	4000
42	MEDLINE	(social AND meaning).ti,ab	3022
43	MEDLINE	exp CULTURE/	94713
44	MEDLINE	COMMUNICATION BARRIERS/	3900

No.	Database	Search term	Hits
45	MEDLINE	barriers.ti,ab	46481
46	MEDLINE	knowledge.ti,ab	296452
47	MEDLINE	39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46	690303
48	MEDLINE	38 AND 47	151
49	MEDLINE	LONDON/	13415
50	MEDLINE	london.ti,ab	18907
51	MEDLINE	49 OR 50	27225
52	MEDLINE	48 AND 51	8
53	MEDLINE	31 AND 51	341

2 Appendix 2: Brent Study Participant Questionnaire

Brent Study

PARTICIPANT QUESTIONNAIRE

Thank you for agreeing to participate in this study. You will be asked a range of questions and your answers will be recorded. The interview should take about 15-20 minutes. I would like to assure you that this is a confidential study which is being carried out to get a better understanding of TB related issues. This is a confidential study and your responses will be seen by the researchers only. Your name will not be provided to any organisation or study and your responses will only be used for the purposes of this study.

How old are you?

Age group Up to 20 Years ❑ 20 – 40 years ❑ 40 – 50 years ❑

50- 60years ❑ Over60 years ❑

1) How long have you lived in the UK? _____

2) Which is your country origin/ birth? _____

3) How would you describe your Ethnic Group?

White European ❑ African ❑ Caribbean ❑ Asian Bangladeshi ❑

Asian Indian ❑Asian Pakistani ❑ Far Eastern ❑ Middle Eastern ❑ Eastern European ❑

Mixed ❑ please describe _____

Other ❑ please describe (ethnicity of the participant)_____

4) Are you currently employed? Yes ❑ No ❑

5) If 'yes ' what is your current occupation _____

6) If no, what was your last job and where? UK or overseas?

7) Are you: single ❑ married ❑ in long-term relationship ❑ widow(er) ❑

8) Educational attainment:

What age did you leave school?

Did you go to secondary school?

Did you attend University?

What is your current profession? _____

Other ❑ please describe

9) Do you have dependant children Yes ❑ No ❑

If yes, how many, and please give their ages _____

10) What kind of accommodation are you currently living in?

Permanent flat or house ❑ Temporary flat or house ❑

Guest of friends or relatives ❑ Squat ❑

Hostel ❑ Where ever I can find ❑ If so, please describe

_____

11) How many bedrooms do you have? _____

12) How long have you lived here?

13) How many people sleep in the same room with you?

14) How many people living in your accommodation?

15) Have you lived abroad during the last three years? Yes ❑ No ❑

If yes, please give details _____

_____

16) Do you share part of your living space with people who are not part of your immediate family? Yes ❑ No ❑

If so, which rooms? _____

With whom? _____

17) Please describe your accommodation type over the last five years, or since you arrived in the UK, including the number of people with whom you shared a room or household.

Time period	Type of accommodation	No. of people	No. of people	
			(in your room)	(In your household)

18) Is your current accommodation in a good state of repair? Yes ❑ No ❑

19) Does your current accommodation have dampness or mould growth?

Yes ❑ No ❑

Who owns your property? Council/private let/housing association? _____

_____

HEALTH

20) Are you registered with a GP? Yes ❑ No ❑

21) Why are you not registered? did you have any problems registering with a GP? Yes ❑ No ❑

If yes, can you say what they were? _____

22) Have you suffered from TB in the past? Yes ❑ No ❑

If 'yes' where were you diagnosed? _____

23) Did you complete your treatment? Yes ❑ No ❑

If no, can you say why?……

……..

……..

Have you been in contact with anyone else who has TB? A relative or friend?

Have you had BCG vaccination?

Visible scar present? Yes/no?

In relation to your recent diagnosis of TB:

24) When did you first begin to feel unwell? _____

25) Did you suffer from any of these?

Fever Yes ❑ No ❑ If 'yes' for how long? _____

Night sweats Yes ❑ No ❑ If 'yes' for how long? _____

Cough Yes ❑ No ❑ If 'yes' for how long? _____

Weight loss Yes ❑ No ❑ If 'yes' for how long? _____

Loss of appetite Yes ❑ No ❑ If 'yes' for how long?

Swelling of glands? _____

Any other symptoms:

_____ _____

_____ **For how long?** _____

_____ **For how long?** _____

For how long?

26) How long after your first symptoms developed did you consult a doctor?

_____

27) If there was delay in seeking advice, what reasons can you give for the delay?

_____

_____

If there was a delay, how long did you delay?

28) What did the doctor advise? Please describe: _____

_____

_____

29) How long after your first symptoms developed were you referred to a TB clinic?

_____

30) How long after your first symptoms developed were you told that you were suffering from Tuberculosis (TB)?

31) Have you had a BCG vaccination? _____

TREATMENT

32) Were you admitted in hospital for treatment? Yes ❑ No ❑

33) If 'yes' for how long? _____

34) When you were discharged from hospital, did you have accommodation to go to that you considered satisfactory? Yes ❑ No ❑

If no, what were the problems about your accommodation?

---

35) How long have you been on treatment? _____

36) Are you getting any side effects from the treatment? Yes ❑ No ❑

37) If 'yes' please describe these: _____

38) Do you pay for your drugs? Yes ❑ No ❑

39) If 'yes', is the payment causing you concern? Yes ❑ No ❑

40) If 'yes' have you ever stopped treatment due to inability to pay? Yes ❑ No ❑

41) Do you think you may stop treatment in the future due to inability to pay? Yes ❑ No ❑

Where do you get the drugs? Clinic or GP?

REACTION TO DIAGNOSIS

42) How did you react to your diagnosis of TB? (Tick all that apply)
I was expecting it ❑, indifferent ❑, anxious ❑, devastated ❑, shocked ❑

or other ❑ (please describe) _____

43) Did you tell your family members about the diagnosis?
Yes❑ No ❑ Not applicable ❑

If not, then why not?……

44) Did you tell your friends about the diagnosis? Yes ❑ No ❑ Not applicable ❑ If not, then why?…….

45) Did you tell your work colleagues about the diagnosis?
Yes ❑ No ❑ Not applicable ❑
If not, then why?……

46) Are you comfortable talking to people about your condition? Yes ❑ No ❑

If not, then why?……..

47) Do you feel your disease is having an impact on your relationship with friends and family? Yes ❑ No ❑

SOCIAL IMPACT OF TB

48) Do you know anyone else who has suffered from TB? Yes ❑ No ❑

49) If your current condition is having an impact on your social life (have you cut down contact with friends and relatives? Yes ❑ No ❑

50) If 'Single' do you think TB will affect your chances of pursuing relationships? Yes ❑ No ❑

51) Has TB affected your employment in any way?

UNDERSTANDING TB

52) Before your recent illness which of the following statements applied in relation to your understanding of TB?

		True	False	Don't Know
1.	**TB is infectious (can be passed from person to person)**	❑	❑	❑
2.	**TB is incurable**	❑	❑	❑
3.	**There is effective non-conventional treatment for TB (i.e. traditional healers)**	❑	❑	❑
4.	**HIV infection increases the risk of TB**	❑	❑	❑
5.	**TB can affect any part of your body**	❑	❑	❑
6.	**TB is hereditary**	❑	❑	❑
7.	**Risk of TB increases in cold weather**	❑	❑	❑
8.	**Smoking increases the risk of TB**	❑	❑	❑
9.	**TB is punishment from God**	❑	❑	❑

Any other comments:

_____

_____

_____

_____

Thank you very much for your time and co-operation.

3 Appendix 3: Focus group schedule: Community Group

1. What do you think causes TB?
2. What is the treatment for TB? Can you talk a little about what you know, and what you have heard?
3. What are the signs and symptoms of TB?
4. Is there any fear about TB in your community?
5. If there is, how is it expressed and talked about?
6. Do you know of anyone who has had TB? What was it like for them?
7. How does your community respond to TB socially? Is it seen as a negative thing?
8. If yes, then what do you think are the reasons for this?
9. What would you do, if you suspect that you have TB?

4 Appendix 4: Ethical Approval Letter

Brent Medical Ethics Committee
Central Middlesex Hospital
The Old Refectory
Acton Lane
Park Royal
London
NW10 7NS
Telephone 020 8453 2461
Facsimile 020 8453 2466

03 May 2005

Ms Amna Mahmoud
Co-ordinator
Brent Refugee Forum
Suite 18, 4th Floor, Chancel House
Neasden Lane
London
NW10 2TU

Dear Ms Mahmoud

Full title of study:	***Knowledge, perception, barriers and the social meaning of Tuberculosis among Asylum seekers ,the homeless and refugee communities in Brent***
REC reference number:	***05/Q0408/20***
Protocol number:	

Thank you for your letter of 11 April 2005, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered by a Sub-Committee of the REC held on consisting of the Chair Catherine Vickery, Dr Kofi Anie and MS Audrey Alimo.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

The favourable opinion applies to the research sites listed on the attached form.

The following typographical errors were high-lighted on the documents submitted. Could you please revise the documents and send them to the Ethics Administrator:

1. In all the Information Sheets please replace "Principle" with "Principal".

2. In the GP Information Sheet under the section "Why Have I been chosen" last Para - "group of GPs, nurses..." should read "groups of GPs, nurses..."

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type:	Version:	Dated:	Date Received:
Application		07/02/2005	07/02/2005
Investigator CV		07/02/2005	07/02/2005
Protocol	1	07/02/2005	07/02/2005
Covering Letter		07/02/2005	07/02/2005
Peer Review Dr Norman Johnson		04/02/2005	07/02/2005
Copy of Questionnaire Community Groups	1	07/02/2005	07/02/2005
Copy of Questionnaire Patients experience	1	07/02/2005	07/02/2005
Participant Information Sheet	2	11/04/2005	12/04/2005
Participant Consent Form	1	07/02/2005	07/02/2005
Response to Request for Further Information		11/04/2005	12/04/2005
Community Focus Groups Questions	1	07/02/2005	07/02/2005
Confirmation of funding		10/01/2005	07/02/2005
Gps and Nurses Information Sheet	1	11/04/2005	14/04/2005
Professional Participants Consent Form	1	11/04/2005	12/04/2005
Structured Interviews for Patients	1	11/04/2005	12/04/2005
GP Questions	1	07/02/2005	07/02/2005
Nurses Questionnaire	1	07/02/2005	07/02/2005
Information Poster		07/02/2005	07/02/2005

Management approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final management approval from the R&D Department for the relevant NHS care organisation.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Notification of other bodies

The Committee Administrator will notify the research sponsor and the R&D Department for NHS care organisation that the study has a favourable ethical opinion.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

05/Q0408/20:	**Please quote this number on all correspondence**

Yours sincerely,

Mona Shah
Committee Administrator

Copy to:

Mr Ricky Banarsee
Brent PCT
116 Chaplin Road
Wembley
MIDDX
HA0 4UZ

5 Appendix 5: Focus group interview schedules

Nurses interview Schedule

1. From your experience what difficulties, if any, do you have dealing with refugees/ asylum seekers?

2. Do you think that you have the knowledge, skills and resources to follow up a TB patient in the community setting?

3. What factors do you consider may have an influence on refugees/ homeless people contracting TB/ finishing their treatment?

4. What factors may affect treatment and follow up of refugee patients and homeless patients?

5. Are you confident in dealing with cultural issues?

6. Do you ever experience any cultural challenges in your practice? Could you give us some examples and how you coped with these?

7. Are you up to date with Immigration Regulation with regard to health service entitlements?

8. How do you feel dealing with a homeless person? What are the difficulties you may face?

9. Are there any questions you feel relevant but we have not asked?

10. Have you any suggestions for improvement of the present situation?

General practitioner interview Schedule

1. Do you think that you have the knowledge, skills and resources to diagnose a case of TB?

2. What factors may delay TB diagnosis, treatment and follow up of refugee patients and homeless patients?

3. From your experience, what difficulties do you encounter dealing with refugees/ asylum seekers in relation to Tuberculosis?

4. Do any cultural issues emerge during consultations that are challenging?

5. Could you give us some examples, and how you dealt with these?

6. Are you confident in dealing with these cultural issues?

7. Are you up to date with Immigration Regulation with regard to health service entitlements? How do the issues of Immigration affect your willingness to register asylum seekers/ refugees with your Surgery?

8. What problems do you encounter in dealing with the homeless?

9. How do you feel registering a homeless person with your surgery?

10. What other factors do you consider may have an influence on refugees/ homeless people contracting TB?

11. Is there any question you feel relevant that we have not asked, that are affecting diagnosis, treatment and compliance with treatment in these groups?

12. Have you any suggestions for improvement on the present situation?

6 Appendix 6: Search History: Tuberculosis and Sunlight

1. MEDLINE; exp CHOLECALCIFEROL/; 20194 results.
2. MEDLINE; (vitamin AND d).ti,ab; 33370 results.
3. MEDLINE; 1 OR 2; 44310 results.
4. MEDLINE; exp TUBERCULOSIS, PULMONARY/; 59678 results.
5. MEDLINE; 3 AND 4; 109 results.
6. MEDLINE; sunlight.ti,ab; 6628 results.
7. MEDLINE; SUNLIGHT/; 9534 results.
8. MEDLINE; 6 OR 7; 13909 results.
9. MEDLINE; 3 AND 4 AND 8; 7 results.
10. MEDLINE; 3 AND 8; 1380 results.
11. MEDLINE; 4 AND 8; 24 results.

7 Appendix 7: Vitamin D and Sunlight study: Assessment of Diet and Sunlight exposure

Ethnicity

What do you consider to be your ethnic background?
Choose ONE section andtick the appropriate box to indicate your ethnic group.

White

❒British & Irish
❒Any Other White background:please write in

Mixed

❒White and Black Caribbean
❒ White and Black African
❒White and Asian
❒ Any Other Mixed background: please write in

Asian or Asian British

❒Indian
❒ Pakistani
❒Bangladeshi
❒Any Other Asian background:please write in

Black or Black British

❒Caribbean
❒African
❒Any Other Black background:please write in

Chinese or other ethnic group

❒Chinese
❒Any other ethnic background:please write in

Which country were you born in? ----------

How long have you lived in England? ----------

Melanin measurements

Pre UV monitoring data
Date of measurement:

Constitutive melanin index (inner upper arm)	Facultative melanin (Back of hand)	Facial Melanin Forehead	Facial Cheek L	Facial R Cheek

Post UV Monitoring
Date of measurement:

Constitutive melanin index (inner upper arm)	Facultative melanin (Back of hand)	Facial Melanin Forehead	Facial Cheek L	Facial R Cheek

Ambient UV Measurements

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8

Personal film measurement

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Date								
Film ID								
Pre exposure								
Post exposure								
SED								
Ambient total SED								

Skin type and Sun Exposure:

How long per day do/did you usually spend outdoors during the daylight hours….

	No time	Less than 15 minutes	15 – 30 mins	30 – 60 mins	1 - 2 hours	3 - 4 hours	More than 4 hours
Last 2 month?							
In Summer?							
In Winter?							

Which one of the 6 categories below best describes your skin type and response to the midday sun in summer months? **(Please circle one)**

Category	Response
1	I have extremely fair skin. I always burn and never tan
2	I have fair skin. I always burn and sometimes tan
3	I have pale coloured skin. I sometimes burn and always tan
4	I have an olive skin. I rarely burn and always tan
5	I have a moderately pigmented brown skin which never burns and always tans
6	I have markedly pigmented black skin which never burns and always tans

Diffey

Category	Response
1	I take care not to expose my skin too long without any protection as I have the sort of skin that burns very easily and, if I'm not careful, the redness can last for several days or more and my skin may peel
2	I don't worry too much about protecting my skin unless I intend staying out for an hour or more as I have the sort of skin that seems to tolerate the sun well, especially after a few days of sun exposure.
3	Sun exposure is not a problem for me as I was born with dark skin and cannot remember getting red, burnt skin from staying in the sun too long.

In sunny weather, both in the UK and in other countries do you……..
(Please tick one box on each line)

	Often	Sometimes	Rarely	Never
a……..protect your skin from the sun, for example with clothing or sun cream	☐	☐	☐	☐
b…….get blistering after being burned in the sun?	☐	☐	☐	☐
c…….actively seek a suntan?	☐	☐	☐	☐

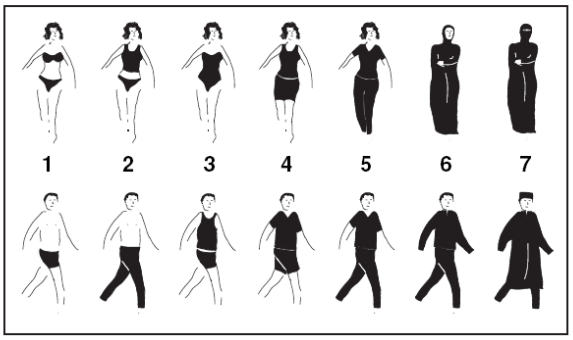
How many times have you used a sun bed in the last year?

	Tick one box
Never	☐
1 to 9 uses per year	☐
More then 10 uses per year	☐

Do you usually wear a headscarf and clothing covering all skin except face and hands (el hejab)? Yes❒ No❒

Sun exposure record

Clothing



Situation

A Outside, not exposed to sunshine
B Outside, partly exposed to sunshine
C Outside, exposed to sunshine
D Outside, no sunshine

Cosmetic use	**Yes**	**No**	**Daily**	**Occasional use**	**Brand name**
Do you use a face cream?					
Do you use a hand cream?					
Do you use a make-up foundation?					

Food Frequency

How often do you eat the following foods? (Please tick one box on each row)

FOOD	More than 4 times a day	2 - 4 times a day	Once a day	3 - 6 times a week	1 - 2 times a week	Less than once a week	Occasi-onally	Never
Margarine								
Oily fish*								
Liver (beef / pork)								
Eggs								
Yoghurt **								
Breakfast cereal **								
Low-fat fortified milk**								

***Examples of oily fish are: tuna, sardines, mackerel, eel, salmon, trout

**** If you eat or drink these products, please write in brand name/s below:

Brand of yoghurt _____

Brand of cereal _____

Brand of low-fat milk _____

Dietary supplements:

In the last month, have you taken any vitamin or mineral supplements, or any cod liver oil or fish oil supplements?

Yes ❒ No❒

If you have answered**YES** please provide details below:

Name of supplement: _____

How often do you take this supplement? (please tick one box)

Once a day or more ❒	**3 to 6 times a week** ❒	**Twice a week or less** ❒	**Not in the last month** ❒

Name of supplement: _____

How often do you take this supplement? (please tick one box)

Once a day or more ❒	**3 to 6 times a week** ❒	**Twice a week or less** ❒	**Not in the last month** ❒

8 Appendix 8: Ethical Approval Letter

RADLO

Moorfields & Whittington Local Research Ethics Committee

Research Ethics Office
Jenner Building
Whittington Hospital
Highgate Hill
London
N19 5NF

Telephone: 020 7288 5676
Facsimile: 020 7288 5674

Ms Senga Steel
Lead Research Nurse
Department of Medicine
Clerkenwell Building
Archway Campus
Highgate Hill
London
N19 5LW

24 June 2005

Dear Ms Steel

Full title of study: **An investigation into the clincial significance of Ultraviolet light exposure,Vitamin D status and Tuberculosis risk in London**

REC reference number: **05/Q0504/30**

Thank you for your letter of 06 June 2005, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information was considered at the meeting of the Sub-Committee of the REC held on 22 June 2005. Ms L Ficker and Mr J Farrell were present at the meeting.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Application	1	09 May 2005
Investigator CV		(None Specified)
Protocol		(None Specified)
Peer Review		(None Specified)
Sample Diary/Patient Card		(None Specified)
Participant Information Sheet	2	10 June 2005

Participant Consent Form	1	09 May 2005
Response to Request for Further Information		06 June 2005
Patient information sheet for contacts	2	10 June 2005
Data on sun exposure		(None Specified)
U/V film badge information		(None Specified)
T Spot-TB information		(None Specified)
GP letter for contact case		(None Specified)
GP letter for index case		(None Specified)

Management approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final management approval from the R&D Department for the relevant NHS care organisation.

Notification of other bodies

The Committee Administrator will notify the research sponsor that the study has a favourable ethical opinion.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

05/Q0504/30	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project,

Yours sincerely

pp

Chair

Email: katherine.clark@whittington.nhs.uk

Enclosures:

Standard approval conditions
Site approval form (SF1)

SF1 list of approved sites

9 Appendix 9: Information leaflet and consent form

Version 3 19/05/09
Information leaflets for participants.

The effects of sunlight on vitamin D levels and Tuberculosis risk in London

What is the purpose of the study?

Research tells us that low levels of Vitamin D in the blood could affect whether a person will develop Tuberculosis or not. Vitamin D is made in the skin when exposed to sunlight and when some foods are eaten such as oily fish. TB in London has increased dramatically over the last ten years and it's important to know what is making people more at risk of developing the disease. It is thought that low levels of sunlight will make some people vitamin D deficient and this will increase their risk of developing TB.

Nobody is really sure if this is true because no one has ever measured exposure to sunshine in people suffering from TB very accurately. We would like to measure the sunshine exposure of those who have TB and the sunshine exposure of people who have been in contact with TB but who are not unwell and then look and see whether there is any difference. We also want to see how this relates to vitamin D levels and how the body deals with Vitamin D; how it is broken down and used by the body.

Why have I been chosen?

You have been chosen because you have been diagnosed with TB

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you wish to withdraw from the study you can do so at any time without giving a reason.

What will happen if I do decide to take part?

The researcher, who is also a nurse will come and see you in the chest clinic to explain the study to you. Next time you come to clinic she will visit you again and ask you whether you would like to take part or not. If you agree to take part a blood sample will be taken from.

you The blood will be used to test your Vitamin D levels and also to confirm your TB diagnosis using a test called Quantiferon Gold. This test is increasingly being used to help doctors diagnose TB more accurately. The test measures the response of your white cells to small proteins called antigens that are produced by the TB bacteria. This can be useful as it is not always easy to tell whether someone has TB or not. Vitamin D is important for health for lots of reasons. These include bone health and increasingly, research is showing that high blood pressure, cancer, diabetes and some neurological disorders have also been associated with Vitamin D deficiency. Because people with dark skins are more likely to become vitamin D deficient, we would also like to know how much melanin you have in your skin. Melanin is the element in your skin that gives it colour. We will take 6 measurements of your melanin index by placing a probe lightly on the bare skin of your inner upper arm. The probe shines a light onto your skin. The amount of light that is absorbed, reflected or scattered within the skin depends on the amount of melanin present. The machine calculates this as the melanin index of your skin. We will then repeat these measurements on the back of your hand and your face. The measurements do not hurt and will cause no discomfort. The researcher will ask you some questions about how long you normally spend outdoors and how much time recently you have been exposed to sunshine and the type of clothing you normally wear.

For the next eight weeks we will ask that you to wear a small clear film badge that you can pin to the outside of your clothing. This film will measure the amount of sunlight you have been exposed to over the eight week period. We can then translate these measurements into a 'sunlight dose' called a 'standard erythemal dose'. We can get the dose by reading the films in a machine called a spectrophotometer. When you have completed eight weeks of wearing the badge, you will be asked to come back to the clinic and give another blood sample that we will test again for Vitamin D and measure your melanin again.

What are the side effects of taking part?

We do not think there will be any side effects of taking part in this study. The blood tests will be a bit uncomfortable and it might be inconvenient wearing the badges

What are the possible benefits of taking part?

There will be no immediate benefit to you but this study may benefit others in the future. It will help us understand how vitamin D and sunlight exposure are influencing the risk of developing TB and will affect what advice health professionals give to people in order to help

prevent it. Knowing whether you have Vitamin D deficiency will provide important information about your general health. If your Vitamin D levels are too low then we will be able to detect this. The researcher will be able to give you basic dietary advice about how you can increase your vitamin D intake through your diet. We will also write to your GP with your permission and suggest a suitable Vitamin supplement for you to correct any deficiency, that your GP will be able to prescribe

What will happen to the results of this research study?

The results of this study will help us understand how sunlight exposure is affecting the risk of developing TB in London and how this relates to Vitamin D levels. We will publish the results of this study in journals and the results will be written up as a thesis that will qualify as a PhD award.

Will my taking part in this study be kept confidential?

Taking part in this study will be kept completely confidential. We will not keep any personal data about you other than your name and address that the researcher will keep in a study file that will be locked in her office. The information will only be used for research purposes.

Who is organising and funding the research?

The Burdett Trust for Nursing is funding the research, which is a charity that supports nursing projects.

What happens if something goes wrong?

We do not think anything will go wrong in this project. We will take every care in the course of this trial. If through our negligence any harm results you will be compensated. However, a claim may need to be pursued through legal action. The NHS Trusts are not permitted to carry indemnity for non-negligent (no-fault) harm.

Contact for further information.

For further information please contact

Senga Steel (RN, MSc)
Principal Investigator
Undergraduate Medical Centre
UCL and Royal Free Medical School
Magdala Avenue

Tel 02072883405

The Whittington Hospital NHS
NHS Trust

Centre Number:
Study Number:
Patient Identification Number for this trial:

CONSENT FORM

Title of Project: An investigation into the clinical significance of the relationship between TB risk, UV exposure and OH hydroxyvitamin D levels in active cases and their contacts

Name of Researcher: Senga Steel

Please initial box

1. I confirm that I have read and understood the information sheet dated……. (version……) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that sections of any of my medical notes may be looked at by responsible individuals from (company name) or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	
Name of Person taking Consent(if different from Researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

1 for participant, 1 for researcher.