Tuberculosis Update

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A World TB Day update on the national and global tuberculosis situation and current UK initiatives contributing to the control of tuberculosis

Introduction from the Chief Medical Officer (CMO)

'On the move against tuberculosis – innovate to accelerate action' sets the theme for World TB Day on 24 March 2010, underlining the importance of innovative thinking and practice in the fight against tuberculosis (TB). This newsletter gives an update on the activities of key organisations to control this disease in the UK and globally. It provides an opportunity to mark the coming event of World TB Day and reflect the concerted efforts of those who are committed to achieving effective TB control.

Figures from the World Health Organization (WHO) suggest that globally the incidence of TB is declining, with an estimated 9.4 million new cases and 1.8 million deaths in 2008. However, preliminary UK data for 2009, presented in this newsletter, indicate a further rise in incidence, with over 9000 new cases.

Developments for improving TB control in the UK continue in a number of crucial areas, as outlined in my 2004 *TB Action Plan*, some of which are highlighted in this newsletter. The Health Protection Agency (HPA), in addition to contributing to frontline services, surveillance and vaccine development, will be launching a National Strain Typing Service in May this year with the aim of enhancing cluster and outbreak investigations.

TB Alert continues with its commitment to raise awareness of TB among affected communities. Simultaneously, the British Thoracic Society, Royal College of Nursing, TB Alert and the All-Party Parliamentary Group on TB have collaborated on the *Second National Tuberculosis Survey of English Primary Care Trusts*. This newsletter also provides an update on other initiatives in TB control, such as identifying effective case management tools, the trialling of an 'opt out' HIV testing policy in TB clinics, and the development of guidelines for detecting and managing TB among hard-to-reach groups.

In keeping with the World TB Day message, I am pleased with the way individuals are collectively striving to stop TB in its tracks. We have made considerable progress, but, nevertheless, still need to scale up vigilance and continue strengthening TB control. I hope the update on the excellent and diverse work outlined in this newsletter proves to be useful and inspirational.

Sir Liam Donaldson
Chief Medical Officer

Please feed back your comments to tbsection@hpa.org.uk

Further guidance on TB can be found on the Department of Health (DH) website: www.dh.gov.uk/en/Publichealth/Communicablediseases/Tuberculosis/index.htm, **and the HPA website:** www.hpa.org.uk/infections/topics_az/tb/menu.htm

UK TB Surveillance - Provisional 2009 Data

In 2009 in the UK, 9153 TB cases were provisionally reported to enhanced national surveillance, a rate of 14.9 per 100,000 population. This represents a 5.5% increase compared with the number of cases provisionally reported in 2008 (see Table overleaf).

The vast majority of reports were from England (92%), where provisional figures increased by 5.3%. Five percent of cases were from Scotland, 2.4% from Wales, and 0.5% from Northern Ireland. Scotland reported a small rise in provisional numbers of 2.9%. Wales and Northern Ireland showed a larger proportional change (an increase and decrease, respectively), though both have shown quite wide fluctuations in provisional reporting in recent years.

In England, London continues to account for the largest proportion of cases reported (41%), followed by the West Midlands (12.3%). A rise in cases was seen in eight out of nine regions, with only the North East showing a decrease (-2%) (see Figure overleaf).

Seventy-three percent of cases were in persons who were born outside the UK, of whom the majority were from South Asia (55%) and sub-Saharan Africa (30%). Only 21% of non-UK born cases were diagnosed within two years of entering the UK. Individuals aged 15-44 years accounted for 60% of reported cases; 21% were 45-64 years old, 15% were 65 years and over and 5% of cases were aged under15 years. Overall, 55% of cases were male, though females made up 54% of cases aged less than 15 years. Fifty-three percent of cases were reported to have pulmonary disease. Of these, 57%

Table: Provisional TB case reports and percentage annual change by country, UK, 2005-2009

Year	Country									
	England		Northern Ireland		Scotland		Wales		Total	
	Number of cases	% annual change	Number of cases	% annual change	Number of cases	% annual change	Number of cases	% annual change	Number of cases	% annual change
2005*	7,768	-	76	-	362	-	164	-	8,370	-
2006	7,942	2.2	61	-19.7	384	6.1	168	2.4	8,555	2.2
2007	7,837	-1.3	65	6.6	401	4.4	193	14.9	8,496	-0.7
2008	7,998	2.1	59	-9.2	455	13.5	167	-13.5	8,679	2.2
2009	**8,423**	**5.3**	**42**	**-28.8**	**468**	**2.9**	**220**	**31.7**	**9,153**	**5.5**

*Note: UK provisional reporting commenced in 2005

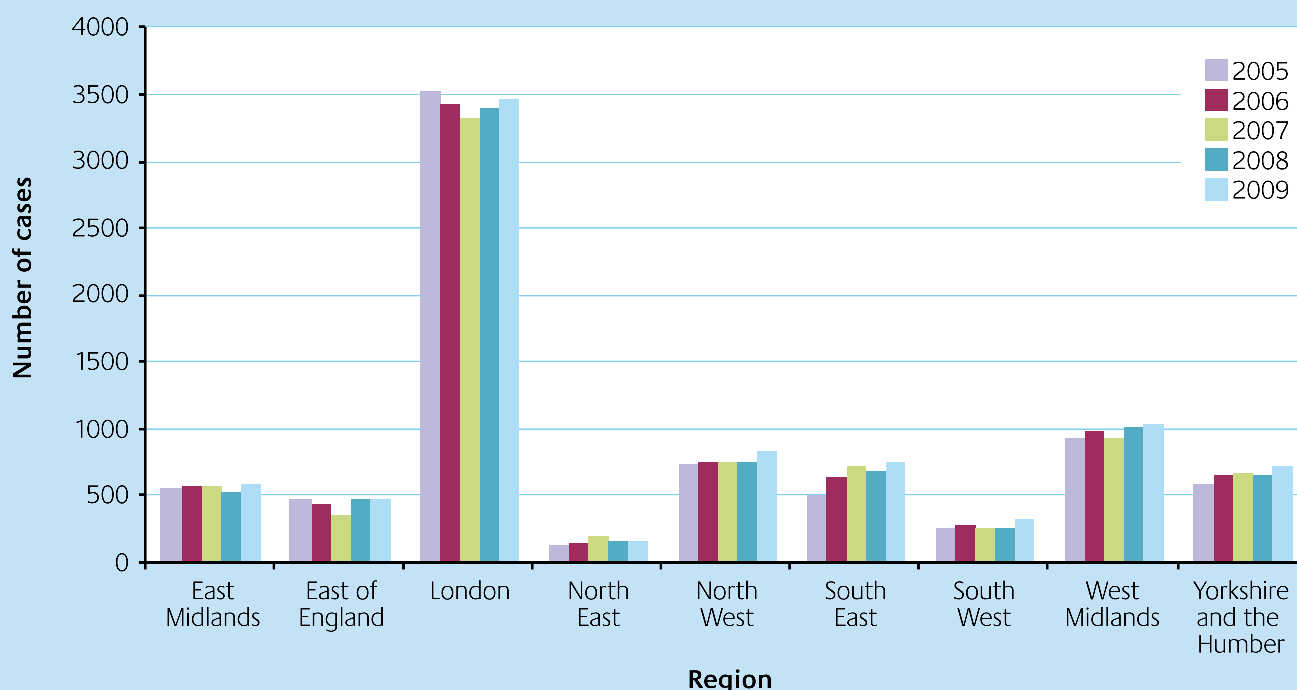
had a reported smear result, of which 57% were sputum-smear positive. These figures are comparable with those reported for the final 2008 data.[1]

The increase observed this year is the highest percentage rise in the number of cases since 2005. The consistent increase over the last decade of enhanced surveillance suggests an underlying true increase in tuberculosis nationally. Efforts to stem the rise, including measures targeting the highest burden areas, should be strengthened. These measures have been detailed in the Chief Medical Officer's action plan published in 2004 and include:

- A high-class clinical service which delivers prompt diagnosis of infectious cases and ensures treatment completion.
- The identification of latently infected persons who are likely to benefit from preventative therapy.
- Innovative approaches, such as DNA fingerprinting to identify areas with the most transmission.
- Identifying high-risk groups, such as immigrants, homeless persons, problem drug users and prisoners, and targeting public health resources to improve the diagnosis and treatment of tuberculosis in these populations.

Provisional data should be interpreted with caution, however, as numbers are likely to change, due to cases being subsequently de-notified as not TB, late notifications, and the removal of duplicate reports during the finalisation of the dataset. It should also be noted that 2009 was the first complete year that the new web-based Enhanced Tuberculosis Surveillance system was operational in England and Wales, which may have improved reporting. Finalised 2009 case reports, including drug susceptibility data, together with treatment outcome reporting for 2008 cases, will be published later this year by the HPA.

Figure: Provisional number of TB cases reported by region, England, 2005-2009



Reference
1. *Tuberculosis in the UK: Annual report on tuberculosis surveillance in the UK in 2009.* London: Health Protection Agency Centre for Infections, December 2009. **www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1259152018585**

Data sources: Enhanced Tuberculosis Surveillance (England, Wales and Northern Ireland) and Enhanced Surveillance of Mycobacterial Infections (Scotland). Rates calculated using Office for National Statistics mid-year population estimates for 2008.

Launch of the National Strain Typing Service

May 2010 will see the launch of the eagerly anticipated National Strain Typing Service. The service was developed in recognition of a need for a comprehensive molecular TB strain typing programme, to inform TB control and target resources more efficiently. The National Strain Typing Service will ensure the provision of a standardised typing system, establish a central database containing both typing and epidemiological data, and provide agreed operational guidelines on the public health use of molecular typing data.

Initially, three HPA laboratories (in Birmingham, London and Newcastle) will provide the strain typing service and all first isolates of *M. tuberculosis* obtained from patients in England will be typed. The service will use the highly specific Mycobacterium Interspersed Repetitive Unit-Variable Number Tandem Repeats (MIRU-VNTR) typing method to discriminate between strains. Cases with identical strain types are highly likely to be linked to an outbreak and this technique can be used to identify clusters of cases derived from a single index case.

Linkage of the Strain Typing Database to the web-based Enhanced Tuberculosis Surveillance system will provide a powerful tool to investigate the growth and characteristics of clusters. This linkage will allow the temporal and geographical distribution of strain types and the demographic and clinical characteristics of cases and their identified contacts to be examined. Information will be used at both national and local levels to facilitate epidemiological investigation of clusters and provide a greater awareness of outbreaks that cross regional boundaries. As the service is rolled out across England, it will enable better control of clusters and support the essential detective work necessary to find contacts of cases and ensure early treatment. Strain typing information will be available in real time to front-line teams to help inform local TB control at the earliest opportunity.

Ultimately, the National Strain Typing Service will greatly enhance our understanding of the dynamics of TB transmission in England and help to strengthen prevention and control. The data generated by this initiative will also advance future research, aiding understanding of the differing transmissibility, virulence and molecular characteristics of TB strains.

Second National Tuberculosis Survey of English Primary Care Trusts

Since 2004, there have been a number of national documents which provide guidance on commissioning and delivering TB services. However, there are no similar standards for TB care, and little in the way of service evaluation. In 2009, therefore, the British Thoracic Society, Royal College of Nursing, TB Alert and the All-Party Parliamentary Group on TB collaborated on the Second National Tuberculosis Survey of English Primary Care Trusts.

The results show that, despite some improvements since the first survey two years earlier, there are still wide variations in levels of service support and clinical practice. Over two-thirds of providers were within a TB clinical network, and almost four-fifths were part of a multi-disciplinary team, yet links to specialist services and local authorities remained generally poor.

Most PCTs expected local numbers of TB cases to rise, and almost all had designated TB leads. However, under half had a TB strategy, with few producing a service level agreement with their local TB provider. Awareness-raising initiatives in high-risk communities were a particular issue for both PCTs and clinical leads.

The survey concluded that most services are still not in line with national recommendations and more needs to be done, if we are to eliminate TB. The importance of links with local authorities and user involvement in planning and delivering a coherent TB strategy were seen as paramount. Also, provider workload requires formal assessment and should be defined within national standards.

It is planned to repeat the survey in two years time, when the focus will also be on quality of commissioning and care.

Local and Regional Services –Tackling TB

Across England, each Health Protection Unit (HPU), along with Regional Epidemiology staff, works with the NHS to deliver services aimed at controlling the spread of TB. Each HPU has two main functions:

- The surveillance, investigation and control of outbreaks.
- To work with NHS commissioners to ensure that local services best meet the needs of the local population.

The HPUs lead the investigation of incidents and outbreaks to support the control of TB. Many of these incidents involve schools and the HPU has a vital role in working with the NHS, local authority and the school to keep parents, governors and students informed and support the action taken in each incident.

The HPUs help the local NHS services find people with infectious TB as early as possible, to reduce the time when they are infectious and ensure that they are treated effectively. TB requires a prolonged course of treatment and sometimes it can be difficult to ensure that people complete their treatment and do not pose a risk of infection to others. Sometimes it may be necessary to use powers under public health law to keep patients in isolation, to protect the public. In such circumstances it is usually HPU staff, working with the local authority, who seek these orders.

Genetic typing of each TB isolate is now helping frontline services pinpoint outbreaks and clusters that would previously have been undetected (see example below and article on the National Strain Typing Service).

Mercian TB – An example of cluster investigation

The largest defined cluster in the Midlands is the 'Mercian' strain of TB. This persistently represents 6% of all typed TB isolates in the West Midlands, but with only a handful of cases elsewhere. With no obvious link between cases, a regional review of routine data was undertaken. So far, this has revealed a demographic profile distinct from that of non-Mercian TB cases, that is, mainly young white or black Caribbean men. Further investigations have helped exclude potential links, such as homelessness, being in prison, or contact with drug treatment services. A hypothesis that transmission might be due to social networks not picked up by routine case investigation is also being explored.

Developing new TB vaccines

Infant Phase IIB efficacy trial of BCG-MVA85A, a collaboration of the Oxford Emergent Tuberculosis Consortium, Aeras and SATVI.

The WHO launched a new Stop TB strategy in 2006 which recognised that, while current tools can control TB, improved practices and elimination will depend on new diagnostics, drugs and vaccines. The Stop TB Partnership Working Group aims to get at least 20 vaccines into Phase I clinical trials by 2015, in order to achieve the goal of one new, safe, effective TB vaccine. Simulation studies indicate that the introduction of a new vaccine in the next five to 10 years could reduce TB incidence in Africa and South East Asia by >20% during the first 10 years of use and by up to 40% by 2050.

The TB group at the HPA Centre for Emergency Preparedness and Response (CEPR) has a major programme of research devoted to TB vaccines, covering vaccine candidate discovery and development, evaluation of third-party candidates and research into biomarkers of disease and vaccine-induced immunity.

The HPA CEPR has the largest TB vaccine evaluation capability in Europe and has conducted key preclinical vaccine efficacy studies for the majority of the lead TB vaccines, enabling their progress into clinical trials. In EU-funded projects between 2003-2009, four candidates were taken to Phase IIB trials and three further candidates prepared for Phase I trials. The main strategy is to increase immunity from BCG by a boost through vaccination. Other promising approaches include modification of BCG by adding immunogenic components, oral delivery of existing BCG strains, and construction of safe and stable attenuations of *M. tuberculosis*.

Currently, CEPR is involved in two new EU initiatives. In NEWTBVAC, CEPR will independently evaluate second-generation TB vaccines. In TRANSVAC, the centre's expertise in animal modelling and immunology will contribute to a generic capability in the development of vaccines (including TB vaccines) to improve public health across Europe. CEPR is also collaborating with colleagues at the Centre for Infections to identify clinically-relevant strains of *M. tuberculosis* against which to screen vaccines.

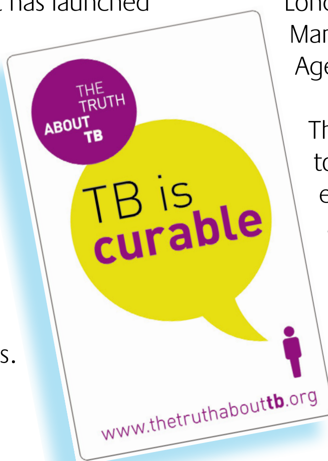
With the first vaccines entering efficacy trials, and a second wave of vaccines in development to tackle different clinical scenarios (including post-exposure and latency), these are exciting times for TB vaccine research and the HPA is at the centre of this global effort.

For more information on the Stop TB global TB research agendas, go to: www.stoptb.org/researchmovement/agendas.asp.

Raising awareness of TB

In his 2004 *TB Action Plan*, the Chief Medical Officer cited 'raising awareness' as the first key action to help bring the disease under control. Raising awareness of TB gets people into treatment sooner and reduces onward transmission, which improves health, saves lives and brings financial savings to the NHS. Awareness strategies need to be targeted primarily at affected communities, especially black African and South Asian communities, homeless people, substance misusers, and prisoners/ex-prisoners.

As the DH's lead partner on raising awareness, TB Alert has launched *The Truth About TB* campaign to provide materials and strategies that can be used by Primary Care Trusts (PCTs), other statutory bodies and voluntary sector organisations. The campaign aims to encourage people to start thinking and talking about TB, addressing underlying social issues that stand in the way of strong TB control programmes.



Central to the strategy is the involvement of voluntary sector organisations – such as those working with Black African communities but which currently focus primarily on HIV issues – so that they can start integrating TB issues into their projects. To help deliver this work, two Community Development Officers will join the TB Alert team this spring; one will be based in London (hosted by Naz Project London in Hammersmith) and the other in Manchester (hosted by the Black Health Agency).

The campaign also aims to bring together key stakeholders to run evaluated pilot projects that develop and demonstrate good practice in TB awareness work. TB Alert will provide guidance, awareness materials and seed funding, and will build on the relationships it has developed with TB networks around the country.

Audience-specific awareness materials will be developed, designed to meet the needs of specific communities. These will build on two 'core' materials: the www.thetruthabouttb.org website and a 10-minute DVD, '*The Real Story*'. The DVD features five people from different backgrounds telling their stories, from first symptoms through to diagnosis, treatment and cure; two experts are also featured and it can be played in 12 languages.

TB Alert has sent a full campaign pack to PCTs and Strategic Health Authorities (SHAs), and you can email resources@tbalert.org or call 01273 234029 for your own pack. This is an innovative approach to raising TB awareness in England, which is vital in reducing the health and economic burden of the disease.

Updates to NICE guidance

TB in hard-to-reach groups

The National Institute for Health and Clinical Excellence (NICE) has been asked by the DH to develop guidance for identifying and managing TB among hard-to-reach groups. For the purposes of this guidance 'hard-to-reach groups' are defined as anyone whose social circumstances or lifestyle makes it difficult to:

- Recognise the clinical onset of TB.
- Access diagnostic and treatment services.
- Self-administer treatment.
- Attend regular appointments for clinical follow-up.

Hard-to-reach groups may be of any ethnicity or country of origin. Factors such as extreme poverty, homelessness, insecure housing tenure, drug addiction and imprisonment can limit access to care and act as important barriers to effective TB control. Delays in diagnosis increase transmission of disease, and lead to poor clinical outcomes. Poor adherence to treatment can lead to prolonged infectiousness, relapse, and development of drug resistant or multidrug resistant disease. The guidance will review published and unpublished evidence to identify effective and cost-effective interventions to tackle the problem.

Consultation on the draft scope was completed on March 9th. The development phase for the guidance will begin in May 2010 and will continue for approximately 16 months. There will be a call for submission of evidence providing an opportunity for stakeholders to submit relevant evidence such as innovative local approaches to the problem. Further details can be found on the NICE website: www.nice.org.uk/guidance/index.jsp?action=byID&o=11978

Diagnosing latent TB

NICE has also been asked by the DH to produce a partial update to the clinical guideline 33: 'Clinical diagnosis and management of TB, and measures for its prevention and control', regarding the use of interferon gamma immunological testing (IGT) in the diagnosis of latent TB.

The guideline will focus on the diagnosis of latent TB by interferon gamma release assays (IGTs) using *M. tuberculosis*-specific antigens (ESAT-6, CFP-10, and TB7.7). It will not look at the diagnosis of active TB, or the treatment of TB.

The diagnostic utility of QuantiFERON-TB Gold In-Tube, QuantiFERON-TB Gold and T-SPOT.TB, alone, or in combination with a tuberculin skin test, will be reviewed and compared with tuberculin skin test alone. The guideline will cover both adults and children in various settings, including both NHS and non-NHS. However, children up to the age of 18 years will be considered as a separate group. Groups to be considered will be:

- Those at increased risk of TB infection, specifically if they were born in, have arrived or returned from high-incidence countries within the last five years, live with, or have close contact with, people diagnosed with active TB, or are homeless and/or problem drug users.
- Those who are immunocompromised, for example, due to prolonged steroid use or HIV infection.
- New and existing NHS employees, occupational healthcare workers, current or former prison inmates, prison and remand centre staff.

NICE will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate.

Further details can be found on the NICE website: http://guidance.nice.org.uk/CG/Wave0/103

Trialling HIV testing in TB clinics in London

Human immunodeficiency virus (HIV) infection poses one of the greatest challenges to tuberculosis control, with recent UK data suggesting an increase in the proportion of tuberculosis cases co-infected with HIV (Ahmed AB. Thorax 2007). New UK guidelines for HIV testing were published in September 2008 by the British HIV Association, the British Association for Sexual Health and HIV and the British Infection Society. These guidelines recommended more widespread HIV testing in clinical services such as TB clinics.

To support the implementation of these guidelines, the National Knowledge Service (NKS-TB) is undertaking a randomised controlled trial. The trial will evaluate the effectiveness of an 'opt out' HIV testing policy and use of new materials for patients and healthcare professionals over a six-month period in 25 London TB clinics. All patients newly diagnosed with TB will be tested for their HIV status, unless they specifically choose not to give their consent. If a patient declines to be tested they will be supplied appropriate information resources to consider and further opportunities to be tested will be offered at their subsequent clinic visits.

Resources have been developed to support this programme in collaboration with representatives from PCTs, respiratory medicine clinics, HIV services and voluntary organisations – TB Alert and National African HIV Prevention. The resources developed include information cards and flip charts (available in 12 languages) for patients, and leaflets to inform healthcare workers about the latest guidelines and help normalise HIV testing in TB clinics. Resources were introduced to the 25 clinics on a stepwise basis between September 2009 and February 2010. Following the study, all resources will be available freely from the NKS-TB website.

For further information on the NKS-TB, see **www.hpa.org.uk/HPA/ProductsServices/InfectiousDiseases/ServicesActivities/1200055718370/**

To find out about case management tools under development, contact **pam.tsangarides@nhs.net**

The APPG on Global TB

The All-Party Parliamentary Group (APPG) on Global TB exists to raise the profile of the global TB epidemic (including the growing incidence of TB in the UK) and help accelerate efforts to meet international TB control targets.

Through its MP and peer members, the APPG strives to raise issues about TB through parliamentary debates and questions and also holds briefings in parliament to provide more in-depth knowledge. Recent briefings have focused on TB-HIV co-infection, TB patients with complex needs, and TB drug resistance. The group also arranges for MPs to visit their local TB service to learn how TB affects their constituency.

The APPG is a member of the UK Coalition to Stop TB – a network of UK organisations established in 2008. The Coalition aims to increase the level of awareness, commitment and political will to address TB through coordinated actions and a unified voice and is a national partner of the global Stop TB Partnership. The 2010 Coalition campaign aims to ensure that the government prioritises TB within its broader health and development agenda.

Further information:
APPG – www.appg-tb.org.uk,
UK Coalition – www.stoptbuk.org/

NHS Evidence-infections, 2010 Annual Evidence Update

In collaboration with the NKS-TB, NHS Evidence-infections has launched its 2010 Annual Evidence Update to coincide with World TB Day.

Annual Evidence Updates (AEUs) are a core part of the work of NHS Evidence-infections. They are produced for the most significant health problems affecting the NHS, and are designed to provide a straightforward and succinct overview of new evidence and guidelines published in the preceding twelve months. The update for World TB Day will be launched on the 22nd of March and include the key guidance, systematic reviews and reports on TB, along with commentaries from experts and useful websites. Find out more at **www.library.nhs.uk/infections.**

NHS Evidence-infections is based at the HPA Centre for Infections, and provides free, convenient and comprehensive access to the best available evidence on the prevention, diagnosis, treatment and control of infectious diseases.

BTS TB Specialist Advisory Group

TB control is a key priority for the British Thoracic Society (BTS). Its Specialist Advisory Group advises the society on matters relating to TB, including the treatment of patients, standards of care and education and research. It also ensures that the society is up to date with, and contributing to, local and national policy.

In 2008, BTS received support from the DH for a new TB project aimed at increasing communication between health care professionals by ensuring that important decisions about treatment and care are not made in isolation. The key elements of this are to support and encourage colleagues to manage TB within a multidisciplinary team (MDT) structure and to develop an online clinical network to facilitate information sharing and best practice.

The 2009 PCT survey (see earlier article) revealed that two thirds of Service Level Agreements between commissioners and providers of TB Services included provision for MDTs. BTS would like to see that figure rise substantially. Rather than imposing a particular structure on MDT groupings, the project aims to encourage what works best in high and low TB incidence areas.

Important insights have already been gained into how colleagues work in MDTs within their own PCTs, and also in wider groupings. This knowledge will be used to develop web-based resources to help new and established groups operate most effectively. The website will also serve as an information hub for other TB-related projects. This, plus the strong links with the HPA, will lead to enhanced clinical care, better education resources, and promote world-beating TB research. For more information, please visit the website www.brit-thoracic.org.uk/tuberculosis.aspx, or email tb@brit-thoracic.org.uk.

Learning from success - TB case management in NYC

In April 2009, five members representing the HPA, London TB Workforce and Find and Treat team, visited New York City (NYC) to observe the proven successful NYC TB case management model. They also undertook training in the cohort review process to inform the implementation and evaluation of an effective case management system to control TB in London.

Members of the London TB Workforce group in NYC

Cohort review is a systematic review of the management of patients with TB and their contacts. A 'cohort' is a group of TB cases counted over a specific period of time, usually three months. Details of the management and outcomes of TB cases are reviewed in a group setting approximately 6-9 months after they are counted in the cohort. The clinical status, treatment outcome, adequacy of the medication regimen, and treatment adherence of each patient are presented by the case manager. This information is collated by the network epidemiologist during the review and presented as an overall outcome for each area against set TB targets, providing on-the-spot feedback to case managers on work efforts. Issues are identified and acted on within 30 days through clear lines of responsibility. This process strengthens evidence-based practice, standardised care and accountability, and has been hugely helpful in the ongoing development of the TB case management system for London.

For presentations on the cohort review process, contact
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For opportunities in cohort review training, contact
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For induction and advice for non-clinical case workers, contact
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