Complications of TB and extra-pulmonary TB

P1 ACCESS TO BEDAQUILINE AND DELAMANID IN ENGLAND FOR TREATMENT OF DRUG RESISTANT MYCOBACTERIAL DISEASE – RESULTS OF A TB SAG SURVEY

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Introduction and objectives Bedaquiline and delamanid were centrally commissioned by NHS England for management of MDR and XDR-TB, within specified criteria (including age 16–65, pulmonary disease, discussion in BTS MDR-TB forum and six months usage) in Aug 2015. We sought to determine ease of availability, obstacles faced and off licence use by prescribing centres.

Methods An electronic survey was sent to the leads or nominated deputy of MDR-TB centres in England, and the responses analysed using the Surveymonkey web tool.

Results Response rate was 64% (18/28). Of the respondents, 8 centres (44%) had not used the drugs since Aug 2015. Of the remainder, indications in all cases were either drug resistance (90% of centres) or intolerance (70% of centres). Intolerance was usually hearing loss from second line injectable agents and tendonitis from fluoroquinolones; a minority of patients also could not tolerate prolonged linezolid. 90% of cases had been discussed in the BTS MDR-TB forum; the exception was a case of non tuberculous mycobacterial(NTM) disease(*M. abscessus*) which was discussed with other NTM experts. There was minimal delay (<2 weeks) between the MDR-TB forum decision to use the drugs and NHS England approval when used for licenced indications; one delay occurred when requesting an extension beyond 6 months (7 weeks delay). There was minimal delay (<2 weeks) between NHS England approval and the patient actually receiving the drug. Both drugs were used in the same patient by two centres (20%). The drugs had been used 'off licence' by 6/10 centres. Details in Table 1. Free text responses highlighted difficulty in obtaining the outcome of individualised funding request decisions, difficulty obtaining funding for children (being paid for by the children's hospital in one case), and two rejections of the use in NTM disease.

Conclusions Access to bedaquiline and delamanid within licenced indications seems to have minimal delay. Difficulties may arise when the drug needs to be used for ≥6 months. Problems are also reported with funding in children. There is emerging evidence of benefit in difficult NTM disease; this is an unlicensed indication that may expand in the future. Consideration may need to be given to a forum for difficult NTM disease.

Abstract P1 Table 1 Off licence use of bedaquiline and delamanid by MDR-TB centres

Reason for off-licence use of bedaquiline/ delamanid	% of centres (note each centre may have more than one off licence usage)	Details
Duration longer than 6 months	30%	All cases pulmonary XDR with large burden of disease and/or limited treatment options
Extra-pulmonary MDR/XDR disease	20%	Lymph node TB
NTM disease	20%	M chimaera sternal wound infection (multiple drug intolerances) and M abscessus extensive pulmonary disease (funding declined by NHS England in both cases, funded by hospital in one case and appeal for compassionate use in the other)
Drug intolerance in fully sensitive disease	10%	Toxic epidermal necrolysis to first line agents

P2 USING AN APP TO DETECT EARLY ETHAMBUTOL TOXICITY

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Aim Ethambutol is one of the first-line drugs used to treat tuberculosis (TB) but its side effects include optic neuropathy, causing sight loss and changes in colour-vision. Early detection can mean any toxicity is reversible. Careful monitoring of sight is therefore required in patients taking ethambutol. After a patient irreversibly lost his sight from ethambutol toxicity and a successful claim was made against the hospital, more robust methods of monitoring eyesight were needed in patients taking ethambutol.

Method Currently in our department, all patients being started on ethambutol are referred to the ophthalmology department for baseline eye testing of visual acuity and colour vision. They are tested again at 4–6 months if they remain on ethambutol past 2 months. In between this, we previously relied on the patient reporting any change in vision to the TB team who would then arrange additional formal testing. To improve monitoring, we purchased two apps- a Munsell D15 Colour Vision Test and a LogMAR acuity test- to be used on an iPad. Four members of clinic staff were trained to use the apps. All patients on prolonged ethambutol now have their vision tested at all TB clinic appointments (usually monthly).

Any change from previous or any problems detected by the apps mean stopping the ethambutol and urgent referral to ophthalmology for formal testing.

Outcomes In six months of using the apps, sixteen patients on ethambutol have had regular testing. Two patients have had changes in vision picked up by the apps. One patient's formal eye testing showed no change. The other showed objective change in acuity and colour vision. Without using the apps, these changes may not have been picked up for several more weeks reducing the likelihood of reversibility. The apps are straightforward and a questionnaire of the staff trained in their use rated them easy to use.

Conclusion By using the apps, additional ophthalmology appointments are avoided unless needed and problems are potentially detected before the patient notices any change in their vision. Early detection enables ethambutol to be stopped with the aim of reversing any optic neuropathy before it becomes permanent.

P3 THE CHALLENGE OF ESTIMATING TB MORTALITY ACCURATELY: RECONCILING DEATHS REPORTED IN THE TB NOTIFICATION SYSTEM AND THE VITAL REGISTRATION SYSTEM IN ENGLAND AND WALES, 2005–2015

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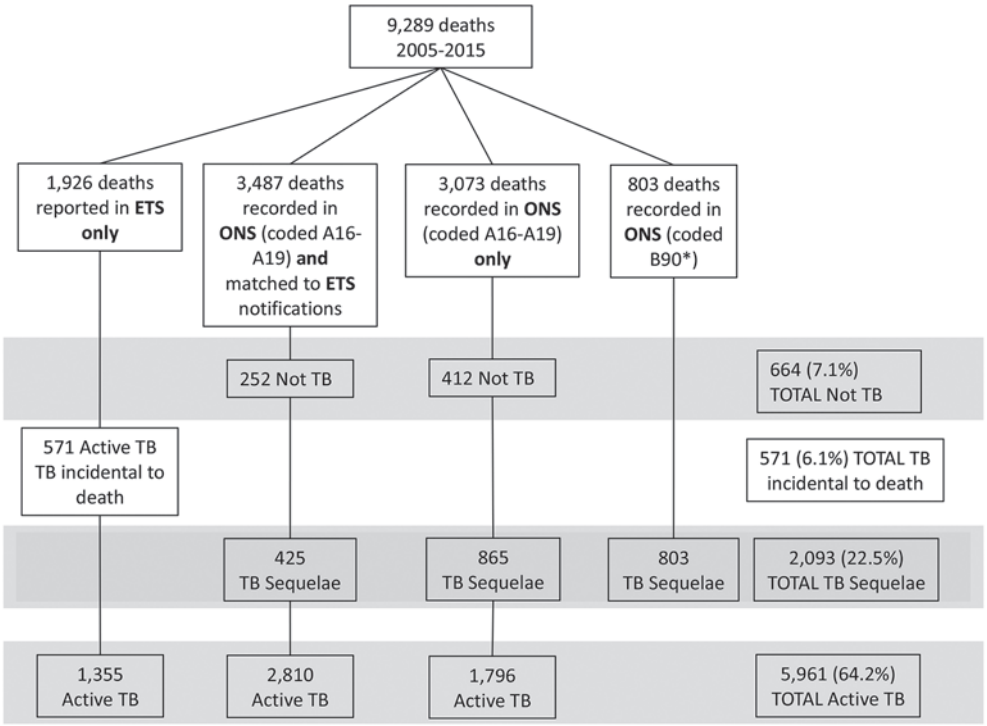
Background An accurate estimate of TB mortality is required to monitor progress towards the end TB goal of reducing deaths by 95% by 2035. In England and Wales (E and W), treatment outcome, including death from all causes, is reported for TB cases notified to the Enhanced Tuberculosis Surveillance system (ETS). The UK Office for National Statistics (ONS) compiles TB mortality statistics from death certificates. We compared data collected in ETS and ONS to inform how best to estimate TB mortality.

Methods TB cases notified in ETS were probabilistically matched to ONS deaths (DONS) between 2005 and 2015 which had ICD-10 codes indicating TB caused or contributed to the death. Deaths reported in ETS (DETS) were identified in DONS to assess if ONS captured all TB deaths. DONS were identified in ETS data to determine if all people dying with TB were notified. Data from ETS and death certificates enabled stratification of deaths into: active TB, TB sequelae and not TB. Risk factors for deaths recorded in only one system were identified with multivariable analysis.

Results In E and W, the number and proportion of DETS (2005: 470 (6.0%), 2014: 364 (5.5%)) was lower than the number of DONS (2005: 654, 2014: 587). 57% of deaths from all causes reported as DETS were recorded as DONS. 53% of DONS were notified as DETS. In total 9289 deaths were identified in one or both systems: 64% were active TB, 23% TB sequelae, 7% were not TB and in 6% TB was incidental. DETS not recorded in ONS were more likely to be culture and smear negative and diagnosed post-mortem. DONS not notified to ETS were more likely to be female, over 65 years old and born in the UK.

Conclusions Data on TB deaths captured in ETS and ONS differ significantly, suggesting neither system captures all TB deaths. Almost one third of TB deaths recorded by ONS are not active TB, and coding changes in ONS could resolve much of this. Further work, including an audit to determine whether there is under notification of TB or incorrect completion of death certificates or both is needed.



Abstract P3 Figure 1 Flow chart of all "TB deaths" identified in ETS and ONS between 2005 and 2015, including details of which have matched to ETS notifications (cases notified between 2000 and 2015). TB deaths classified into active TB, TB sequelae, not TB and TB incidental to death.