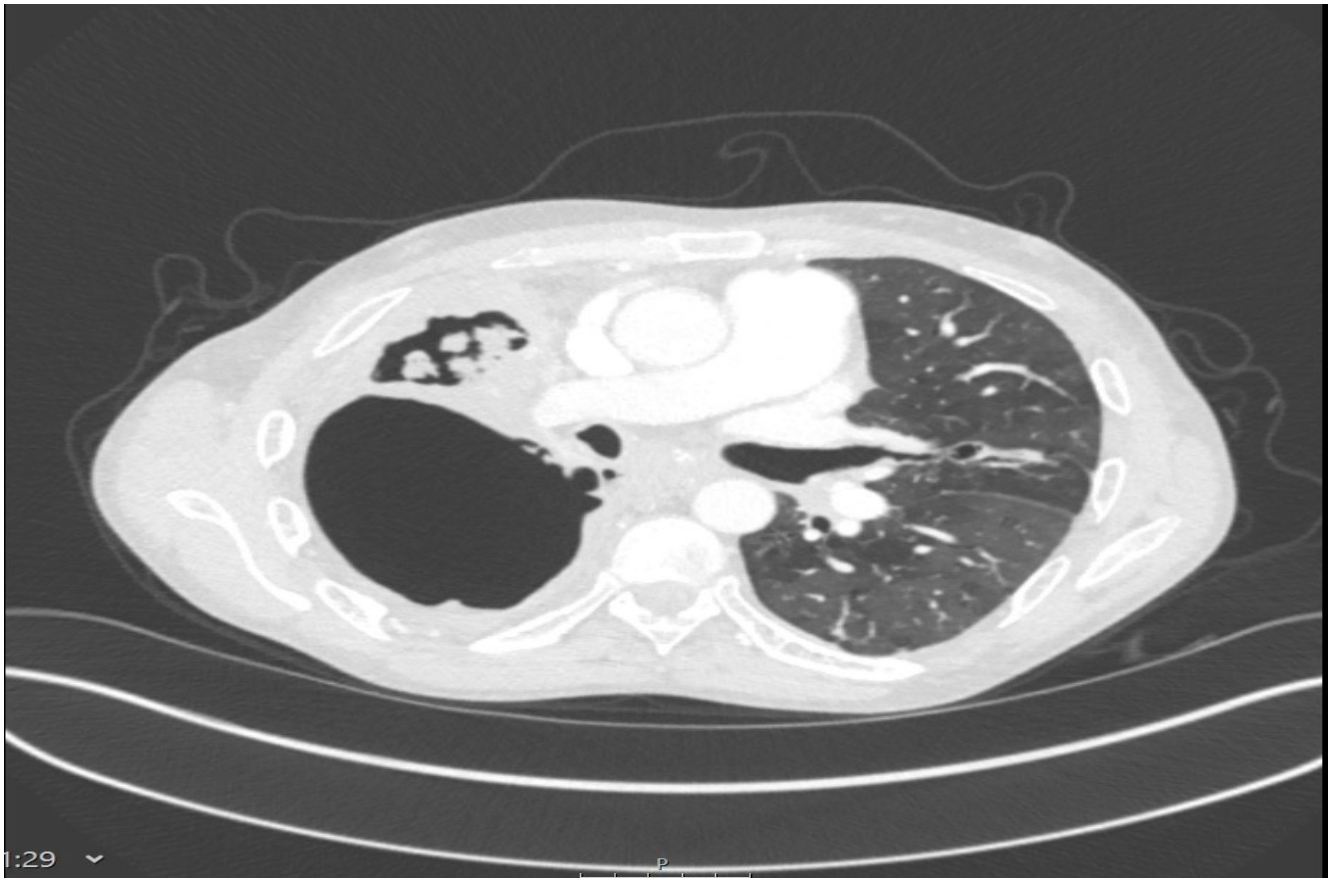
BTS MDR-TB Clinical Advice Service Annual Report 2023



December 2023, ISSN 2040-2023
British Thoracic Society Reports
Vol 14, Issue 3, 2023

EXECUTIVE SUMMARY

The BTS MDR-TB Clinical Advice Service was launched in January 2018 with the intention of fulfilling three key objectives: Facilitating the provision of expert advice on the treatment and monitoring of multidrug-resistant tuberculosis (MDR-TB); increasing the understanding of drug toxicity patterns across the UK and providing a formal gatekeeping function for the use of specially commissioned and novel drugs.

Provision of expert advice to clinicians

See Overview 1 (page 12): Service Activity in Numbers

The Service facilitates the provision of advice on a case-by-case basis. From July 2021 to June 2023 our panel of expert Clinical Service Advisers (CSAs) had advised on 236 cases, of which over 36% were reported as known or suspected MDR/XDR-TB. Many other cases involved sensitive TB that was functionally MDR due to toxicity.

Clinical Service Advisers provided 1,861 written advice messages to clinicians in this period, often within hours of a case being posted. Monthly teleconference multidisciplinary team (MDT) meetings were also used to discuss 85% of cases, with treating clinicians invited to dial in to provide extra detail and ask additional questions. Interested observers from trainees and the wider TB community are also invited to dial in to the monthly virtual MDT meetings.

Drug toxicity patterns in the UK

Clinicians using the Service provide details of the reasons for ceasing treatment with each drug. In 2021 the reported toxicities were published as *The MDR-TB Drug Toxicity in the UK 2021.* This report (available on the BTS website), has proved a valuable reference tool for UK-wide drug toxicity patterns and the intention is to release future updated versions.

Gatekeeping function – specialised commissioned and novel drugs

See Overview 2 (page 20: Specialised Commissioned and Novel Drugs)

Finally, the Service provides an independent review and consensus on supporting Blueteq applications for the use of bedaquiline and delamanid. In the reporting period, 82% of cases involving XDR, MDR or suspected MDR-TB have had one or more of these drugs recommended. This important gatekeeping function is likely to expand as bedaquiline use increases and with the introduction of other high-cost therapies such as pretomanid.

Impact of the Clinical Advice Service

Expert clinical advice on the treatment and monitoring of cases of MDR-TB (and similar infections) or complex functionally resistant TB has a direct and immediate impact on patient care. These cases are increasingly complex, and the impact of prompt, expert clinical, microbiological, and public health advice cannot be overstated.

The BTS MDR-TB Clinical Advice Service forms a crucial resource supporting the care of patients both directly and indirectly. Wider implications of the Service include facilitating ongoing training and development of the TB workforce. As the important work of this Service continues it is anticipated that further benefit will also be realised through research activities.

The Service makes an essential contribution to promoting education for both attending clinicians and CAS advisors, through knowledge exchange and shared clinical experience of treating MDR-TB. We have recorded 66 person-hours of clinician involvement in MDTs over 24 months (for their own cases). However, we have not quantified the time many clinicians remain in the MDT after their own case has been discussed, which is common. Anecdotal feedback is that the MDTs provide a valuable learning opportunity for clinicians and expert advisers alike.

The MDTs also serve an important role supporting the training of Higher Specialty Trainees in Respiratory Medicine and Infectious Diseases. This has a wider implication for the future of the workforce. Over the reporting period, we recorded 188 person-hours of trainee/observer involvement. We are actively exploring ways to expand the scope of virtual learning offered by the Service in the future.

Through the BTS Data Access Request Process, launched in January 2020, researchers are able to request access to pseudonymised data which would ultimately help improve patient care.

Early in 2023 ethics approval was granted for the MDR-TB Clinical Advice Service by the Research Ethics Committee (REC) for a second term of 5 years. Changes to the Service in the latest REC approval include the inclusion of patients who do not have the capacity to provide consent. Additionally, for patients who do have the capacity to consent, agreement to additional processing of data for the purpose of research has changed from opt-in to opt-out.

CONTENTS

FOREWORD

The Multidrug-Resistant Tuberculosis Clinical Advice Service has been providing direct support to clinicians for five years, having a real and immediate impact on the treatment of patients with the most complex and challenging cases of tuberculosis across the UK. From January 2018 to June 2023 a total of 582 cases were discussed through the Service, covering XDR and MDR-TB, other complex TB and non-tuberculous mycobacterial infections (NTMs).

The involvement of a multi-disciplinary team (MDT) is essential to providing the best and most appropriate treatments for the patients in our care. Respiratory and infectious disease physicians, paediatricians, microbiologists, public health consultants, pharmacists and TB nurses all bring complementary knowledge and experience into the Service, and we are very fortunate that our colleagues volunteer their time so generously. This MDT way of working not only improves patient care but also continuously improves our own knowledge and understanding. This also provides a rich resource for the ongoing education of trainees across several specialties.

Through the Service we now routinely discuss around 100+ new cases a year, giving advice on drug regimens, toxicity management, public health measures and non-medical interventions. The excellent engagement we have from microbiology colleagues at reference laboratories also means that whole genome sequencing data are at the core of our discussions. This additional detailed information and discussion allows for critical information that often provides 'game-changing' management choices as well as public health interventions.

Regimens used to treat patients with complex or drug-resistant TB involve multiple drugs, many of which are themselves toxic. When a patient experiences an adverse reaction to their TB treatment it can be challenging to determine which drug might be responsible; this supplemental report provides a rapid way to identify the likeliest causal agents. Managing adverse reactions is key to improving the quality of life and outcomes for patients.

The MDR-TB Clinical Advice Service is a core component of the TB Action Plan for England. NHSE has supported the BTS MDRTB CAS for over 5 years and funding for the period 2021-25 has been approved in recognition of its significant contribution to the most complex cases across the UK.

This report describes the cases supported by our panel of expert advisers from July 2021 to end of June 2023, highlighting the importance of this national resource in improving the care of MDR and complex TB patients in the UK.

Professor Onn Min Kon
Chair, BTS MDR-TB Clinical Advice Service Steering Group

The BTS MDR-TB Clinical Advice Service plays a vital role in minimising the impact of drug resistant TB on patients and their carers and communities. Now in its 5th year in this format, it continues to be a key tool in reducing the impact of TB where management is complex. It plays a vital role in education, the optimal use of novel treatments and prompts additional scientific research.

The dedicated website offers clinicians faced with the most challenging TB cases, unrivalled access to prompt, collaborative, expert advice. This current report shows that the number of new cases referred to the service is growing year-on-year, highlighting increased awareness. There has also been growth in the educational role of the service which will ultimately lead to better care for people with MDRTB.

The Clinical Service Advisers are drawn from respiratory medicine, infectious diseases, paediatric medicine, TB nursing, pharmacy, public health and microbiology and I am immensely grateful for the time, care, and expertise they so generously volunteer.

Dr Paul Walker
Chair, BTS Board of Trustees (*2021-2024*)

BTS MDR-TB Clinical Advice Service Steering Group Membership 2023:

Professor Onn Min Kon	Chair
Dr Toby Capstick	Consultant Pharmacist
Dr Suzi Coles	UK Health Security Agency representative
Dr Martin Dedicoat	British Infection Association (BIA) representative
Professor Marc Lipman	British HIV Association (BHIVA) representative
Dr Felicity Perrin	Chair of the BTS TB Specialist Advisory Group (SAG)
Dr Esther Robinson	National Mycobacterial Reference Service (NMRS) representative
Professor Gerry Davies	BTS Consultant member
Lynn Altass	NHSE (Corresponding member)
Dr Heinke Kunst	BTS Consultant member
Dr Pranabashis Haldar	BTS Consultant member
Miss Sally Welham	BTS Chief Executive
Mr Miguel Souto	BTS Head of Clinical Programmes
Miss Maria Loughenbury	BTS Lung Disease Registry Manager
Miss Suzanne Howard	BTS MDR-TB CAS Coordinator

ACKNOWLEDGEMENTS

The BTS MDR-TB Clinical Advice Service received initial funding from Public Health England (PHE) for the year 2017/18. Funding to support the continued operation of the Service was received from NHS England for the years 2021-2025. This support is gratefully acknowledged.

We would also like to acknowledge the Clinical Service Advisers who generously volunteer their time and expertise, without which the Clinical Advice Service would not be able to run. A full list of the Clinical Service Advisers who have supported the Service from 2021-2023 is included on page 22.

If you would like to know more about the BTS MDR-TB Clinical Advice Service, please visit the BTS website at: https://www.brit-thoracic.org.uk/quality-improvement/lung-disease-registries/bts-mdr-tb-clinical-advice-service/

Cover photograph: CT scan of a patient with pulmonary tuberculosis.

INTRODUCTION

The management of MDR-TB is more complex and associated with more adverse effects than standard TB treatment. The complexity of cases is broad, and a substantial proportion of patients have health, social or economic circumstances that confound their treatment and contribute to poor outcomes. The cost of treating MDR-TB is extremely high (at least 10 times that of drug sensitive TB), in part due to prolonged isolation in hospital and costly alternative anti-mycobacterial drugs.

There are four primary routes through which the Service works with to improve patient care:

- **Facilitating the provision of advice to clinicians**
  After written patient consent is obtained, clinicians may post their case to the Clinical Advice Service. Cases posted are reviewed and once approved by the Service administrator, the panel of expert Clinical Service Advisers (CSAs) are notified that a new case has been posted to the Service. The CSAs can review the anonymised case details, providing prompt advice on treatment and offer continued monitoring through the website.

  Additional support is provided via formal and structured, monthly, virtual multidisciplinary team meetings (MDTs). Treating clinicians are strongly encouraged to attend, providing an opportunity for real-time discussion with CSAs to reach an informed consensus for optimising patient care.

- **Providing an expert opinion on the use of specialised commissioned and novel drugs**
  One role of the panel of CSAs is to consider the appropriateness of the use of specialised commissioned and novel drugs. When clinicians make an Individual Funding Request (IFR), the CSAs advise on the appropriateness of this. When bedaquiline or delamanid funding is requested through the Blueteq system, applicants are asked to confirm discussion in a regional MDT and hence the MDR CAS provides this resource by real-time responses and monthly MDTs. The national TB plan now advocates that all MDR cases are discussed with the MDR CAS. A minimum of three CSAs must approve the proposed regimen containing both or either of these drugs.

- **Supporting research**
  All patients whose cases are discussed must give consent for their data to be processed for that purpose. Separately, patients are advised that their anonymised data may be used for the purpose of research, unless they choose to opt out. In 2020 BTS launched a data access request process, through which researchers from external organisations may apply to access pseudonymised data. For more details about the BTS Data Access Request Process please visit:
  https://www.brit-thoracic.org.uk/quality-improvement/bts-clinical-data-policy-and-data-access/

- **Increasing knowledge and understanding of drug toxicity patterns**
  In addition to providing clinicians with the tools needed to make the best clinical decisions for their patients, the intention is for the Service to support care across the UK by improving the understanding of drug toxicity patterns. To this end a supplemental report, *MDR-TB Drug Toxicity in the UK*, was published for the first time in 2021. The supplemental report includes a full breakdown of the clinician-reported reasons for ceasing treatment with each drug and gives a guide to the possible culprits for each of the most common adverse effects experienced by patients.

This report is intended to provide an overview of the Clinical Advice Service along with the cases which have been discussed through the Service and, as a useful resource, will be updated periodically.

Who can participate in the BTS MDR-TB CAS and how many are doing so now?

The BTS MDR-TB Clinical Advice Service is open to all secondary and tertiary care institutions in England, Scotland, Wales, and Northern Ireland, as well as the island territories (Crown Dependencies). At the end of June 2023, over 540 clinicians had registered to use the Service and cases had been entered from a total of 158 sites across the UK. Overall, 582 cases had been discussed through the Service from January 2018 to June 2023.

Clinicians may bring cases of consenting patients with confirmed or suspected drug-resistant tuberculosis, as well as other complex tuberculosis or mycobacterial infections, to the Service for discussion. Data entry for individual patient records is divided into three sections:

- Patient demographic information (age, gender, comorbidities, etc.).
- Clinical features at the time the case is first brought to the Service.
- Follow-up information from subsequent clinic visits.

Service Ethics Approval, Information Governance and Data security

New ethical approval for the British Thoracic Society Multidrug Resistant Clinical Advice Service Database (22/LO/0698) was granted by the London – South East Research Ethics Committee (REC) in November 2022. This continues the 2017 REC approval stating that patient consent must be obtained before any patient information is entered into the BTS MDR-TB CAS. Information for patients and copies of the dataset are available on the BTS website at:
https://www.brit-thoracic.org.uk/quality-improvement/lung-disease-registries/bts-mdr-tb-clinical-advice-service/

All patient identifiable data (e.g. name, date of birth) are encrypted at the point of entry and visible only to the hospital team in the centre responsible for treating the patient. The British Thoracic Society Information Governance Policy and associated data security policy documents are available on the BTS website at: https://www.brit-thoracic.org.uk/about-us/governance-documents-and-policies/

Availability of advice through the MDR-TB CAS

The British Thoracic Society created the platform on which the MDR-TB Clinical Advice Service is provided to facilitate discussion between health care professionals in relation to individual patient cases of confirmed or suspected MDR-TB (or other complex TB/mycobacterium infections).

Neither the British Thoracic Society nor the MDR-TB Clinical Advice Service has any clinical responsibility or accountability for the patients that are discussed. The posting facility and reports provided are intended to support the clinician and to this end they are provided with a variety of experienced opinions and discussion to inform optimal clinical decision making, and this does not constitute medical advice from BTS. It remains the responsibility of the referring healthcare professionals involved in the Service to make decisions appropriate to the circumstances of each patient in consultation with the patient and or their guardian/carer.

Notes on data and percentages/denominators

Throughout this report figures are displayed as percentages and as exact figures (of the format *numerator/denominator*). When reading this report please be aware that:

- Denominators in this report always exclude cases where no response was entered.
- Unless otherwise stated, denominators in this report exclude cases where the saved response was ‘not known’ or ‘not recorded’.
- Percentage figures are rounded to the nearest whole number throughout this report. This means rounding errors may lead to some total percentages adding up to, for example, 101%.

PART 1 – The Impact of the BTS MDR-TB CAS

The BTS MDR-TB Clinical Advice Service has a number of real-world benefits. As well as directly supporting clinicians with advice, the Service has significant impacts on the TB workforce:

- **Supporting UK MDR-TB experts** by fostering closer ties among the expert community across the UK. The panel of expert advisers also includes a mix of new and more senior advisers, identifying and supporting the development of MDR-TB and NTM experts.

- **Supporting and developing trainees** by providing the opportunity to observe expert national multidisciplinary discussions, increasing, and maintaining clinical expertise.

The monthly virtual MDTs, which facilitate real-time discussion of individual cases, also have another important dimension: education. When treating clinicians dial in to discuss their own cases, they often observe the other case discussions. Clinical Service Advisers have described the MDTs as a unique opportunity for them to discuss a range of complex MDR-TB and NTM cases, and to learn from colleagues across a range of specialist areas.

> The MDR-TB Clinical Advice Service brings together superb experience and leadership to provide outstanding service to clinicians and their patients. My own experience involves a challenging and difficult case of NTM-PD and I found the process and advice excellent.
>
> **Dr David Connell, Consultant Physician in Respiratory Medicine, Honorary Senior Lecturer, University of Dundee**

The BTS MDR-TB CAS across the UK

The BTS MDR-TB Clinical Advice Service was developed with the intention of supporting clinicians in the treatment and monitoring of patients across all four nations of the UK and the island territories (Crown Dependencies).

Since the launch of the Service in January 2018 clinicians have submitted cases of MDR-TB (and similar infections) to the BTS MDR-TB Clinical Advice Service from hospitals across England, Scotland, Wales, Northern Ireland, and the Isle of Man.

Cases of MDR-TB are more commonly treated in major cities, such as London and Birmingham. The geographical distribution of cases submitted to the CAS highlights the importance of sharing local expertise and experience nationally. Figures 1 and 2 (page 10) illustrate the increase in the number of regions submitting cases since the CAS launch.

Figure 1: 2018 Locations of submitted cases

Location of centres which brought at least one case to the BTS MDR-TB CAS from January 2018 - July 2019

Figure 2: Current Locations of submitted cases

Location of centres which brought at least one case to the BTS MDR-TB CAS since the Service launch in January 2018 – July 2023

The History of the BTS MDR-TB CAS

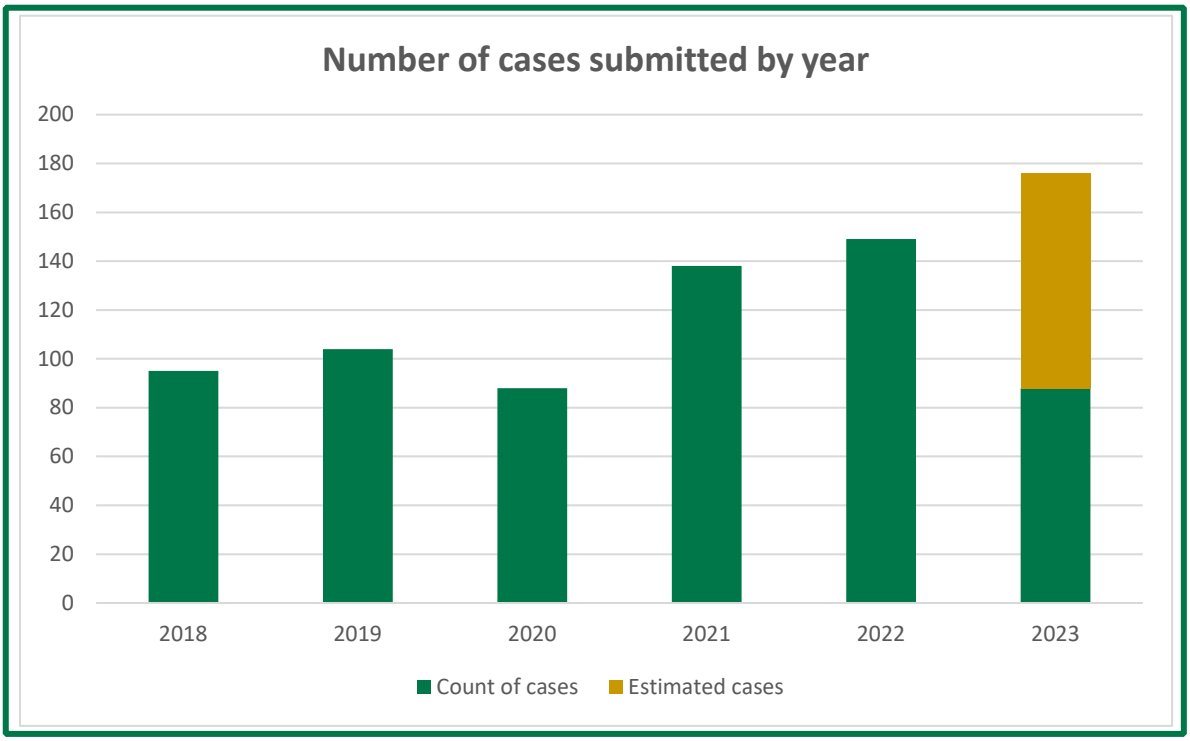
The BTS MDR-TB Clinical Advice Service launched in January 2018, building on the longstanding work of the previous MDR-TB Forum.

The original MDR Advisory Service Forum was launched in 2008, with Professor Peter Davies as the lead physician. This service was a huge step forward in the management of MDR-TB in the UK, providing a means of centralising case discussion. From 2011 this forum was managed by BTS, with Drs John Watson and Martin Dedicoat acting as lead clinicians. This forum included fully anonymised patient data only.

The forum was very well received and provided an essential resource for clinicians. As a direct result of the success of this forum a new service was planned, expanding on the work of the existing forum. This new BTS MDR-TB Clinical Advice Service was launched in January 2018, formally collecting a range of patient information crucial for the provision of advice and essential for understanding patterns of drug toxicity in the UK. The number of cases received by the service has seen year on year growth, with a noticeable dip recorded in 2020 due to Covid-19.

Figure 3: Cases in the MDR Clinical Advisory Service over time

This chart shows the increase in numbers of cases discussed through the BTS MDR-TB Clinical Advice Service over time, for all categories of disease (including NTM and complex sensitive TB). Cases are counted in the year they were first discussed and numbers for 2023 are shown as actual (period January-June) and then a projected total to the end of year.



Overview 1: Service Activity in Numbers

When the BTS MDR-TB Clinical Advice Service was launched the intention was to provide an expert service that was responsive to the needs of clinicians. This overview provides a brief summary of the activities of the Service for the reporting period of July 2021 to June 2023.

543 clinicians are registered on the Clinical Advice Service from a total of **158** hospitals across all four nations of the UK, and the Isle of Man

44

Expert Clinical Service Advisers

- Respiratory medicine
- Pharmacy
- Paediatrics
- Infectious diseases
- TB nursing
- Public health
- Microbiology

236

Cases discussed by our panel of expert advisers

8 XDR-TB

46 MDR-TB

32 Suspected MDR-TB

22 Resistant non-MDR-TB

NTM **62**

Other/Unknown **15**

Other complex TB **17**

Complex sensitive TB **34**

1,861

Individual messages from expert Clinical Service Advisers to clinicians who have posted cases. These messages are separate to the MDT discussions, and initial responses are often received within hours.

Discussion is a key element in identifying the best approach to treatment and monitoring for each individual case.

Of all cases brought to the BTS MDR-TB Clinical Advice Service have been discussed at our monthly virtual MDTs*. The remaining 15% were provided with advice without requiring MDT discussion.

* Excluding new cases with discussion pending at the end of June 2023.

26 Virtual MDTs were held, with a mean of 15 cases discussed per meeting. Cases may be discussed at MDT as often as needed.

68
Hours of **MDT** discussion, with one MDT every month

66
Person-hours of **clinician MDT involvement.** This assumes 20 minutes per case, whereas many clinicians stay on the call for much longer (as a learning opportunity)

934
Person-hours of **adviser MDT involvement**. Our expert advisers gave their time, knowledge and experience voluntarily

188
Person-hours of **trainee / observer MDT involvement**

Recorded Abstracts:

- Manalan K, Altass L, Capstick T, *et al.* (2022) S82 The British Thoracic Society multi drug resistant TB clinical advice service activity: 2018–2022 summary *Thorax* **77:**A51.
- Lipman M, Altass L, Capstick T, *et al.* (2022) P5 Increasing NTM caseload within the BTS MDR TB national clinical advice service: the tip of an iceberg? *Thorax* **77:** A82-A83.

PART 2 – Multi and Extensively Drug-Resistant Tuberculosis (MDR AND XDR-TB)

This section of the report deals with cases reviewed from July 2021 to the end of June 2023, initially categorised by the clinician as being either XDR-TB, MDR-TB or suspected MDR-TB.

The World Health Organisation (WHO) definitions, as of January 2021[1]:

Pre-XDR-TB: TB caused by Mycobacterium tuberculosis(M.tuberculosis) strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone*

XDR-TB: TB caused by Mycobacterium tuberculosis (M. tuberculosis) strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug*

*The fluoroquinolones include levofloxacin and moxifloxacin as they are the fluoroquinolones currently recommended by WHO for inclusion in longer regimens. The Group A drugs are currently levofloxacin or moxifloxacin, bedaquiline and linezolid, therefore XDR-TB is MDR/RR-TB that is resistant to a fluoroquinolone and at least one of bedaquiline or linezolid (or both). The Group A drugs may change in the future; therefore the terminology Group A is appropriate here and it will apply to any Group A drugs in the future.

From July 2021 to June 2023, 38 centres have contributed cases classified by the treating clinician as either XDR, MDR or suspected MDR-TB to the BTS MDR-TB Clinical Advice Service:

118 patient demographic records

147 complete clinical/diagnosis records

27 follow-up records representing 21 unique patients.

2.1 THE MDR/XDR-TB PATIENT COHORT

Over half (60%) the patients were male, and the majority were of either White (30%), South Asian (30%) or Black African (18%) ethnicity.

The mean age of patients at the time their case was first discussed on the CAS was 34.2 (± *16.0*), with ages ranging from 1 to 90. More than half of patients (63%) were aged 20–39 years.

Over half of patients (52%, 43/83) had no listed clinical risk factors. Where present the most common were smoking, diabetes and hepatitis B. Immunosuppression was also reported in just short of 20% of cases, with a third of those reporting biological therapy (anti TNFα) as the cause. Three cases of immune-suppression were due to HIV co-infection (overall 3% of the population had HIV co-infection).

The majority (93%, 92/99) of patients had no listed social risk factors. Of those who did the most common were alcohol addiction (43%), prison history (14%), and where drug use was a known risk factor, (1 patient - 14% of cases) that patient was still actively using drugs.

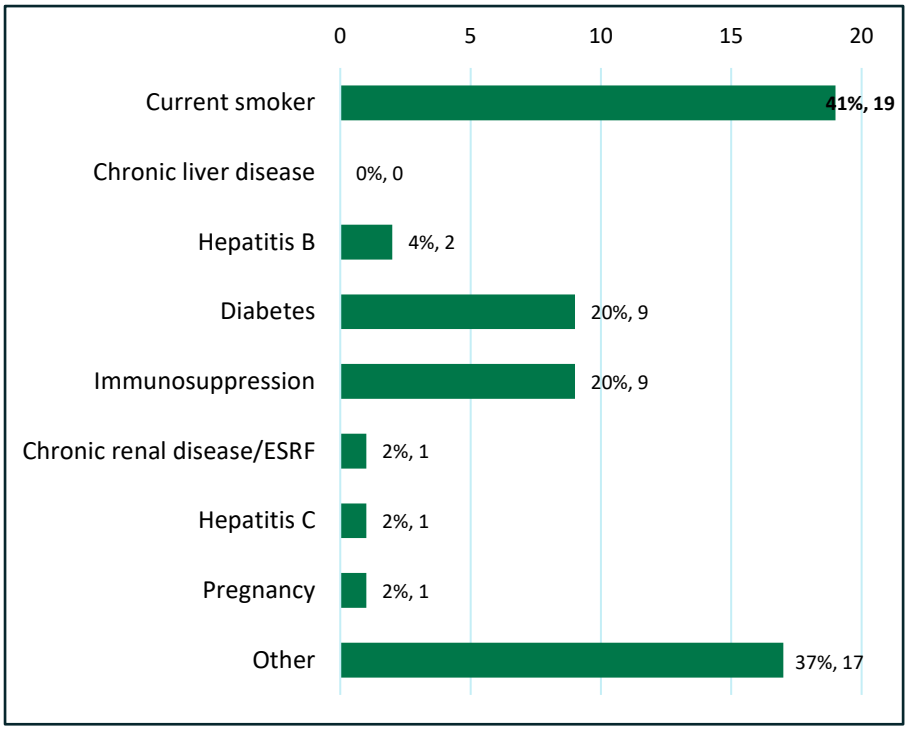


Figure 4: Clinical risk factors at first discussion (Total records:46)
Clinical risk factors recorded for all patients with known or suspected MDR/XDR-TB from July 2021 to the end of June 2023.

Overall, nearly a quarter (23.4% (26/111) of the cases discussed between July 2021 and June 2023 involved a patient who was known not to be in work. Occupation categories where the risk of exposure to TB may be elevated include education (15% of all cases) and healthcare (6%)

2.2 CLINICAL/DIAGNOSTIC DATA

Cough (60%), weight loss (49%), fever (36%), fatigue (30%) and producing sputum (28%) were the most commonly reported symptoms. Overall, 8% (8/108) of screened patients were reported to be asymptomatic. The majority of patients (87%) experienced symptoms for between one and six months before their case was entered onto the Service. No patients reported experiencing symptoms for over a year.

Excluding sputa, where smear samples were obtained the most commonly reported techniques were lymph node aspirate (5.6% of cases) and bronchoalveolar lavage (BAL) /endobronchial washing (4.6% of cases).

Overall, 69% (79/115) of cases had pulmonary involvement, with extra-thoracic and intra-thoracic lymph node involvement (26% and 19%) and pleural disease (5%) also frequently reported.

Overall, 22% (27/118) of patients were known to have a previous diagnosis of TB. Of these, 18% (22/118) involved active and 4% (5/118) latent TB.

Key Figures

- **69%** of cases had pulmonary involvement
- **8%** of patients asymptomatic
- **22%** previously diagnosed with TB *(18% active, 4% latent)*
- **68%** required contact tracing
- **8%** did not identify if any contact tracing was required
- **57%** had therapy observed in some way (e.g. DOT/VOT)

Contact tracing was required in 68% (71/105) of cases, while contact tracing requirements were unreported in 8% (8/105) of cases. Therapy was directly observed (DOT) in 32% (27/85) and video observed (VOT) in 25% (21/85) of cases. Therapy was self-administered (SAT) in 35% (30/85) of cases.

2.3 DRUG RESISTANCE

Local molecular laboratory capacity was responsible for 96% of cases (63/66) of initial MTB identification by PCR, with rpoB mutation representing rifampicin resistance present in 93% of cases where known (70/75).

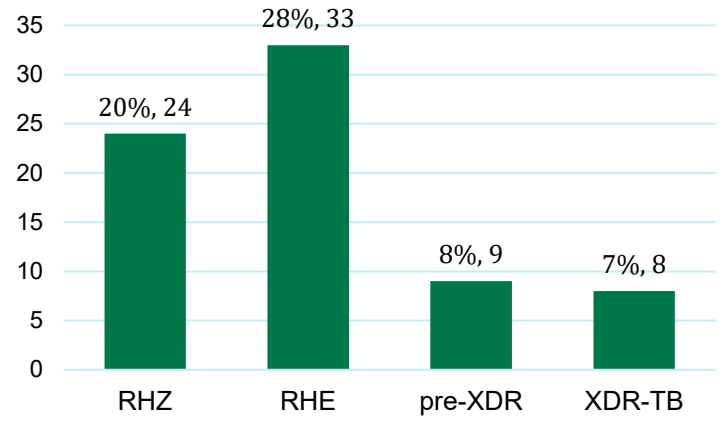


Figure 5: Clinician-reported resistance pattern
Resistance patterns as reported by clinicians. These figures do not draw from whole genome sequencing (WGS) data.

Of the 118 patients known or suspected XDR/MDR-TB (as described by the treating clinician), 20% (24/118) were specifically reported as resistant to each of rifampicin (R), isoniazid (H), and pyrazinamide (Z), and 28% (33/118) to R, H and Ethambutol (E).

Using the 2021 World Health Organisation (WHO) definitions[1], 8% (9/118) of cases would be considered to meet the definition of pre-XDR TB, and 7% (8/118) of cases met the definition for full XDR-TB.

PART 3 – Complex Sensitive TB and Drug Resistant Non-MDR TB

This section of the report deals with cases reviewed from July 2021 to the end of June 2023, initially categorised by the clinician as being either complex sensitive TB, drug resistant non-MDR TB or other complex TB. The cases included in this section were contributed by 74 different centres.

88 patient demographic records

88 complete clinical/diagnosis records

26 follow-up records representing 16 unique patients.

3.1 THE COMPLEX SENSITIVE/RESISTANT NON-MDR TB PATIENT COHORT

Patients were predominately female (57%, 49/86), and the majority were of either South Asian (39%), White (33%), or Black African (11%) ethnicity.

The mean age of patients at the time their case was first discussed on the CAS was 41.1 (± *17.3*), with ages ranging from 5 to 80. Close to half of patients (42%,37/88) were aged 20 – 39.

Over a quarter of patients (26%, 17/66) had no listed clinical risk factors. Where present the most common were immune-suppression, diabetes and smoking. Cases where immunosuppression was a factor, biological therapy (anti TNFα) was the cause in 47% (8/17) of cases. Two cases of immune-suppression were due to HIV co-infection (overall 8% of the population had HIV co-infection).

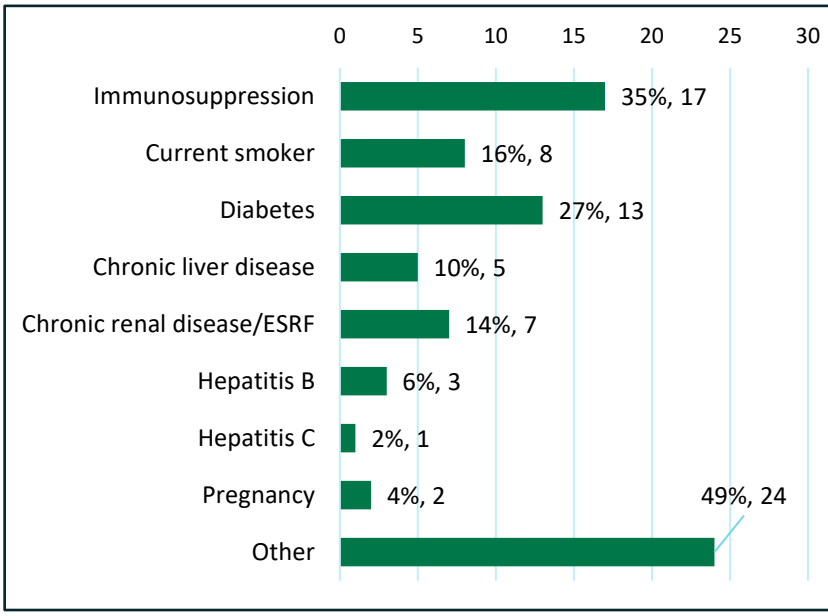


Figure 6: Clinical risk factors at first discussion
Clinical risk factors recorded for all patients with complex sensitive TB or resistant non-MDR TB from July 2021 to the end of June 2023.

The majority (70%, 70/79) of patients had no listed social risk factors. Of the few listed the most common were homelessness (56%, 5/9) alcohol addiction (44%,4/9), and prison history (22%, 2/9).

Overall, 37% (32/86) of the cases discussed between July 2021 and June 2023 involved a patient who was known not to be in work. Occupation categories where the risk of exposure to TB may be expected to be elevated were healthcare (7% of cases), social services/prison sector workers (1%) and education (9%).

3.2 CLINICAL/DIAGNOSTIC DATA

Cough (65%), weight loss (52%), fevers (48%), fatigue (43%) and producing sputum (35%) were the most commonly reported symptoms. Overall, 13% (3/79) of patients were reported to be asymptomatic. The majority of patients (84%) experienced symptoms for between one and six months before their case was entered onto the Service, with 11% of patients experiencing symptoms for a year.

Excluding sputa, where smear samples were obtained the most common techniques reported were bronchoalveolar lavage (BAL) /endobronchial washing (3% all cases) and lymph node aspirate (3%).

Overall, 81% of cases had pulmonary involvement, with intra-thoracic and extra-thoracic lymph node involvement also frequently reported (27% and 23%).

Overall, 5% (4/88) of patients were known to have a previous diagnosis of TB. Of these, 3% involved active TB and 1% involved latent TB.

Key Figures

- **13%** of patients asymptomatic
- **5%** previously diagnosed with TB *(3% of which were active TB)*
- **33%** required contact tracing
- **47%** had therapy observed in some way (e.g. DOT/VOT)

Contact tracing was reported as required in 33% (8/24) of cases. Therapy was directly observed (DOT) in 39% (10/26) and video observed (VOT) in 8% (2/26) of cases. Therapy was self-administered (SAT) in 54% (14/26) of cases.

PART 4 – Specialised Commissioned and Novel Drugs

NHS England has commissioned the use of bedaquiline (Bdq) and delamanid (Dlm) for the treatment of MDR-TB and XDR-TB in patients who meet the following criteria:

- Treatment agreed following discussion with the MDT of the MDR-TB treatment centre or the regional MDT in conjunction with an MDR-TB treatment centre; treatment of children must also be agreed after discussion with a Paediatric Infectious Diseases Centre.
- The patient must be managed under directly observed therapy.
- The treatment regimen must be designed according to current WHO recommendations[2], based on known resistance patterns and tolerance to individual drugs.

The BTS MDR-TB Clinical Advice Service can be considered as providing the function of a regional/national MDT to consider support of Blueteq applications for the use of these drugs.

The information presented here relates to individual patient treatment history at first entry. Data on the panel supporting the prescription (or continuing use of) bedaquiline or delamanid is based on the outcome of virtual MDT case discussion meetings and – on a small number of occasions – support through consensus reached outside MDT discussion.

These figures cover the period of July 2021 to the end of June 2023 (unless otherwise stated). WHO guidance upgrading bedaquiline to a Group A agent was released in 2018, then in 2020 bedaquiline was listed as replacing injectables in the short course treatment.

Of the 279 cases registered with the BTS MDR-TB CAS, 50% (137/279) involved a clinician requesting support to use bedaquiline (95%,130/137), delamanid (2% 2/137) or both bedaquiline and delamanid (2%, 2/137) or either bedaquiline or delamanid (2% 3/137).

Overall, the panel recommended at least one of bedaquiline and delamanid in 48% (135/279) of all cases. Of these 82% (111/135) were made in response to requests from the clinician (representing 81%, 111/137, of clinician requests), and 18% (24/135) were made in the absence of any clinician request.

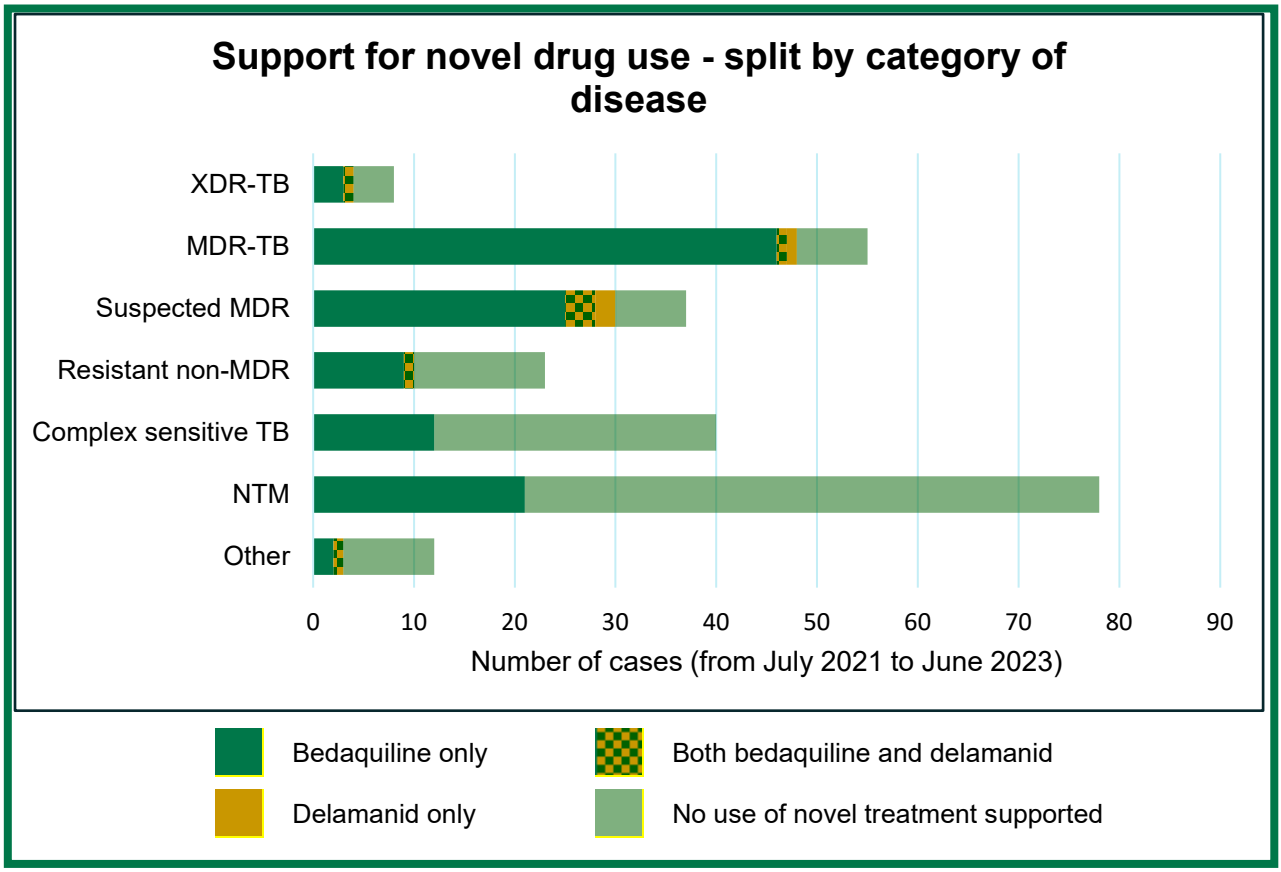
Key Figures

- **50%** of all cases involved a clinician seeking to use bedaquiline, or bedaquiline and delamanid
- The panel supported using Bdq and/or Dlm in **48%** of all cases, and in **88%** of cases of known or suspected XDR/MDR-TB
- The panel supported concomitant use of Bdq and Dlm in **13%** of all XDR-TB cases
- Support for the use of Bdq has increased over time, as expected from the WHO Guidelines promoting Bdq to Group A agent

The use of bedaquiline without delamanid was more likely to be supported (93%, 125/135) than delamanid (2%, 3/135) or combined bedaquiline and delamanid therapy (5%, 7/135), across all categories of disease. Support for combined therapy generally occurred in cases with extensive drug resistance or intolerance patterns, where very limited effective drug options were available. Concomitant use of bedaquiline and delamanid was supported in 13% (1/8) of all XDR-TB cases discussed. A full breakdown of support for the use of bedaquiline and/or delamanid is included in Overview 2 (page 20).

Overview 2: Specialised Commissioned and Novel Drugs

The BTS MDR-TB Clinical Advice Service provides an important gatekeeping function for the use of specialised commissioned and novel drug therapies, conducting independent reviews and providing consensus on whether to support use (or continued use beyond 24 weeks) of bedaquiline and delamanid.



This figure shows the absolute numbers of cases discussed during this reporting period, as reported at entry to the Service. Further analysis is required to determine the eventual categorisation of cases reported as suspected MDR-TB.

The proportion of cases where the panel supported the use of one or more novel drug treatments is high (82% of cases reported to have known or suspected XDR/MDR-TB). Considering the gatekeeping function of the Service, these data highlight the essential role of expert discussion in case management.

These figures may be artificially low, as cases where advisers indicated conditional support (e.g. dependent on pending sensitivity results, or on the loss of another drug) have not been counted.

	Bedaquiline only	Both bedaquiline and delamanid	Delamanid only	No use of novel treatment supported
XDR-TB	38% (3/8)	13% (1/8)		50% (4/8)
MDR-TB	83.6% (46/55)	2% (1/55)	2% (1/55)	13% (7/55)
Suspected MDR-TB	68% (25/37)			19% (7/37)
Resistant non-MDR	39% (9/23)			57% (13/23)
Complex sensitive TB	30% (12/40)			70% (28/40)
NTM	27% 21/78)			73% (57/78)
Other	17% (2/12)			75% (9/12)

CLINICAL SERVICE ADVISERS

We would like to extend our sincere thanks to all the expert Clinical Service Advisers (CSAs) who have generously volunteered their time:

Dr Eliza Alexander
Dr Sarah Anderson
Dr Amber Arnold
Dr Lucy Baker
Dr David Bell
Professor Graham Bothamley
Dr Toby Capstick
Miss Aneeka Chavda
Ms Christabelle Chen
Dr Suzi Coles
Dr Ian Cropley
Professor Gerry Davies
Dr Martin Dedicoat
Professor Francis Drobniewski
Dr Laura Ferreras Antolin
Dr Elena Ferran
Professor Andres Floto
Dr Ana Gibertoni Cruz
Mr Mark Gilchrist
Dr Tom Gorsuch
Dr Louis Grandjean
Dr Guy Hagan
Dr Pranabashis Haldar
Dr Izak Heys
Ms Hanna Kaur
Dr Merav Kliner
Professor Onn Min Kon
Dr Deepti Kumar
Dr Heinke Kunst
Dr Ian Laurenson
Dr Patrick Lillie
Professor Marc Lipman
Miss Vikki Lloyd
Dr Jim Macfarlane
Dr Ingrid Madzikanda
Dr Sophia Makki
Dr Andrew McCallum
Dr Olga Moncayo
Professor David Moore
Dr Stephen Morris-Jones
Dr Sarah Mungall
Dr Camus Nimmo
Dr Omar Pirzada
Dr Poonam Puthran
Dr Padmasayee Papineni
Dr Esther Robinson
Dr Andrew Rosser
Dr Georgina Russell
Dr Uli Schwab
Dr James Seddon
Dr Delane Shingadia
Dr Derek Sloan
Professor Grace Smith
Dr Simon Tiberi
Dr Clare van Halsema
Dr Naomi Walker
Dr John Watson
Dr Steven Welch
Dr Natasha Weston
Dr Elizabeth Whittaker
Dr Stephen Wilson
Dr David Wyllie

REFERENCES

1. World Health Organisation. Meeting report of the WHO expert consultation on the definition of extensively drug-resistant tuberculosis (2021)
   [Available from: https://www.who.int/news/item/27-01-2021-who-announces-updated-definitions-of-extensively-drug-resistant-tuberculosis accessed 30/08/2023]

2. World Health Organisation. WHO consolidated guidelines on drug-resistant tuberculosis treatment (2019)
   [Available from: https://apps.who.int/iris/rest/bitstreams/1211676/retrieve accessed 04/112021]

BTS

Further information on the work of the British Thoracic Society can be found on the following websites:

British Thoracic Society (BTS)

BTS MDR-TB Clinical Advice Service

Respiratory Futures