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.

Impact of the Clinical Advice Service

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

Education is essential, with clinicians gaining experience in treating MDR-TB. We have recorded 30 person-hours of clinician involvement in MDTs over 18 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. Anecdotal feedback is that the MDTs provide a valuable learning opportunity for clinicians and expert advisers alike.

Specialist trainee involvement in MDTs also has a wider implication for the future of the workforce. Following an initial trial period where four person-hours of trainee involvement were recorded in virtual MDTs (from April to June 2020) trainee involvement has been expanded. We are actively exploring ways to improve the educational impact of the Service in the future.

It is also anticipated that the Service will facilitate research through the BTS Data Access Request Process, launched in January 2020. This allows researchers to request access to pseudonymised data for research (from patients who have specifically consented to this use) which would ultimately help improve patient care.

Provision of advice to clinicians

See Overview 1: Service Activity in Numbers

The Service facilitates the provision of advice on a case by case basis. From January 2018 to June 2020 our panel of expert Clinical Service Advisers (CSAs) had advised on 242 cases, of which 57% were known or suspected MDR/XDR-TB. Many other cases involved sensitive TB that was functionally MDR due to toxicity.

Over 1,250 written advice messages were sent to clinicians, often within hours of a case being posted. Monthly virtual multidisciplinary team (MDT) meetings were also used to discuss 90% of cases, with treating clinicians often dialling in to provide extra detail and ask additional questions. These virtual MDT meetings were originally held by telephone, but these are now held using videoconferencing facilities.

Drug toxicity patterns in the UK

See Overview 2: Drug Toxicities

Clinicians using the Service provide details of the reasons for ceasing treatment with each drug. Reported toxicities are published in our annual report, forming a resource which may be referenced by clinicians.

Gatekeeping function – specialised commissioned and novel drugs

See Overview 3: 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. Overall 53% 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 novel therapies such as pretomanid.

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

British Thoracic Society

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 from January 2018 to June 2020.

300 clinicians are registered on the Clinical Advice Service from a total of **75** hospitals across all four nations of the UK, and the Isle of Man

43

Expert Clinical Service Advisers

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

242

Cases discussed by our panel of expert advisers

- **15** XDR-TB
- **89** MDR-TB
- **34** Suspected MDR-TB
- **24** Resistant non-MDR-TB

- NTM **32**
- Other **18**
- Other complex TB **11**
- Complex sensitive TB **19**

1,254

Individual messages from expert Clinical Service Advisers to clinicians who have posted cases

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

BTS MDR-TB Clinical Advice Service 2020

90%

Of all cases brought to the BTS MDR-TB Clinical Advice Service have been discussed at our monthly virtual MDTs*. The remaining 10% were provided with advice without requiring MDT discussion.

* Excluding 12 new cases with discussion pending at the end of June 2020.

32

Virtual MDTs were held, with 10-12 cases typically discussed per meeting. Cases may be discussed as often as needed.

62

Hours of **MDT discussion.** One two-hour MDT every month, plus two *ad hoc* MDTs for cases which were especially complex

30

Person-hours of **clinician MDT involvement** since this was first recorded in January 2019

550

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

4

Person-hours in an initial trial period of **trainee MDT involvement** over three months

We circulated a survey to UK clinicians with an interest in TB. 88% of respondents were aware of the BTS MDR-TB CAS and 63% had used the Service in the preceding 12 months.

100%

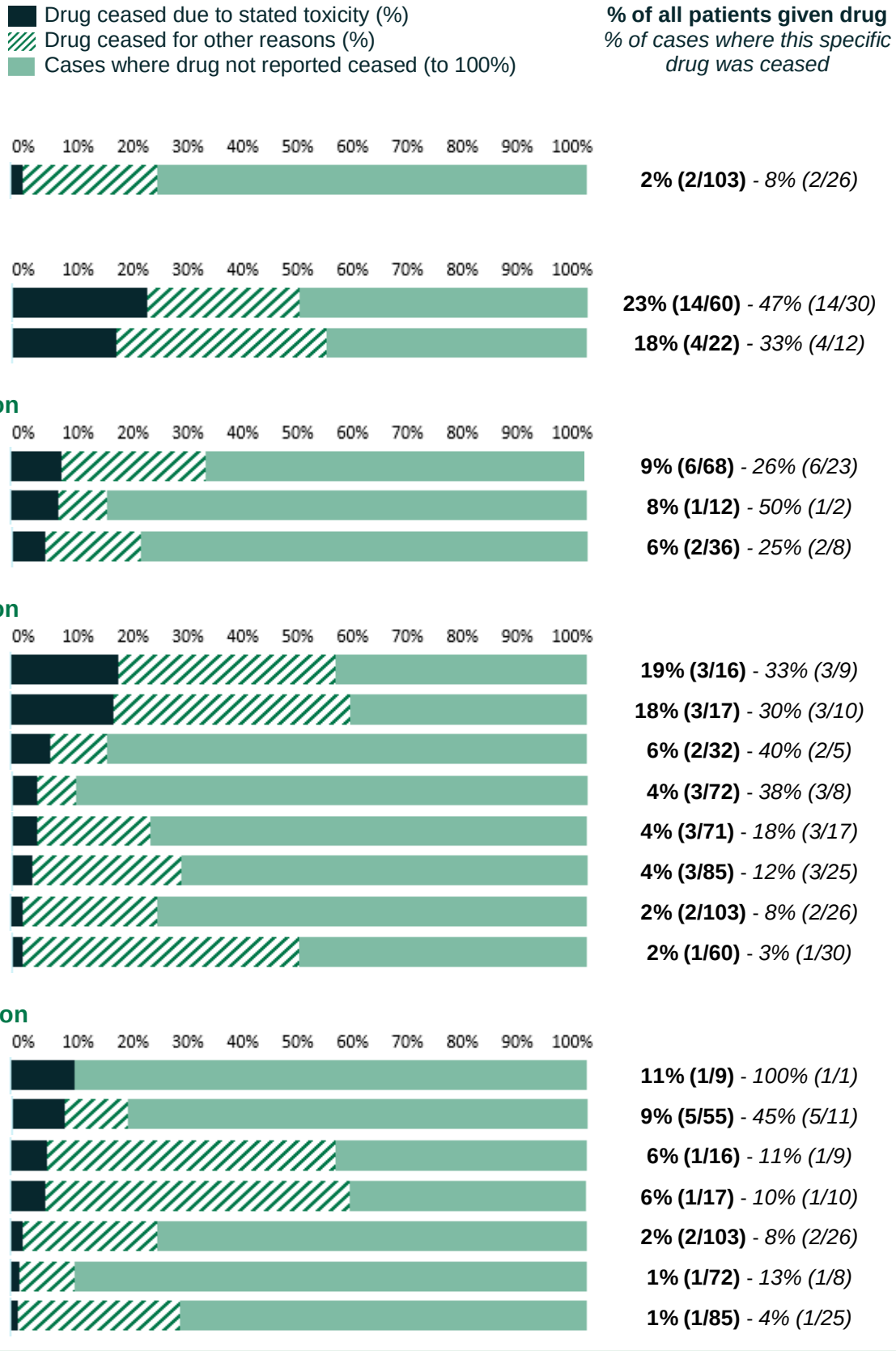
Of clinicians found the advice to be clinically useful when they responded to our survey in late 2019

- 83% said that 80-100% of their MDR cases were discussed through the Service
- 96% of clinicians would use the Service again
- 89% of clinicians described the MDTs as good or excellent

British Thoracic Society

Overview 2: Drug Toxicity

This figure gives an overview of reported drug toxicity for cases of XDR, MDR and suspected MDR-TB from January 2018 to June 2020. Bars represent total cases where each drug was given (100%) with proportions shown for cases ceased due to the stated toxicity (navy) or other reasons (striped).



% of all patients given drug
% of cases where this specific drug was ceased

Arthralgia

Pyrazinamide (Z)	**2% (2/103)** - *8% (2/26)*

Audiological reaction

Amikacin (Am)	**23% (14/60)** - *47% (14/30)*
Capreomycin (Cm)	**18% (4/22)** - *33% (4/12)*

Cardiovascular reaction

Moxifloxacin (Mfx)	**9% (6/68)** - *26% (6/23)*
Delamanid (Dlm)	**8% (1/12)** - *50% (1/2)*
Bedaquiline (Bdq)	**6% (2/36)** - *25% (2/8)*

Dermatological reaction

Meropenem (Mpm)	**19% (3/16)** - *33% (3/9)*
Co-amoxiclav (Amx/Clv)	**18% (3/17)** - *30% (3/10)*
Levofloxacin (Lfx)	**6% (2/32)** - *40% (2/5)*
Clofazimine (Cfz)	**4% (3/72)** - *38% (3/8)*
Cycloserine (Cs)	**4% (3/71)** - *18% (3/17)*
Linezolid (Lzd)	**4% (3/85)** - *12% (3/25)*
Pyrazinamide (Z)	**2% (2/103)** - *8% (2/26)*
Amikacin (Am)	**2% (1/60)** - *3% (1/30)*

Gastrointestinal reaction

PAS	**11% (1/9)** - *100% (1/1)*
Prothionamide (Pto)	**9% (5/55)** - *45% (5/11)*
Meropenem (Mpm)	**6% (1/16)** - *11% (1/9)*
Co-amoxiclav (Amx/Clv)	**6% (1/17)** - *10% (1/10)*
Pyrazinamide (Z)	**2% (2/103)** - *8% (2/26)*
Clofazimine (Cfz)	**1% (1/72)** - *13% (1/8)*
Linezolid (Lzd)	**1% (1/85)** - *4% (1/25)*

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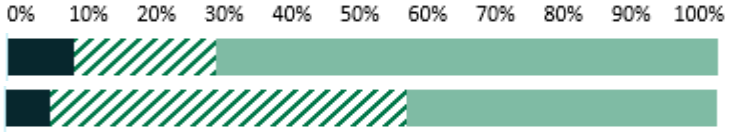
Drug ceased due to stated toxicity (%)
Drug ceased for other reasons (%)
Cases where drug not reported ceased (to 100%)

% of all patients given drug
% of cases where this specific drug was ceased

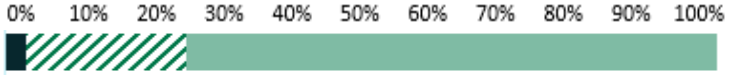
Haematological reaction



Linezolid (Lzd) — **9% (8/85)** - *32% (8/25)*

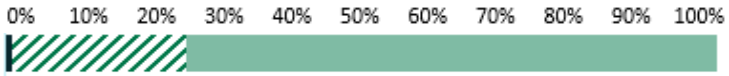
Meropenem (Mpm) — **6% (1/16)** - *11% (1/9)*

Hepatic reaction



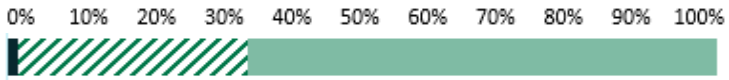
Pyrazinamide (Z) — **3% (3/103)** - *12% (3/26)*

Hyperuricaemia



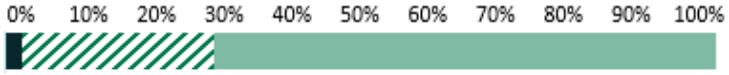
Pyrazinamide (Z) — **1% (1/103)** - *4% (1/26)*

Immunological reaction



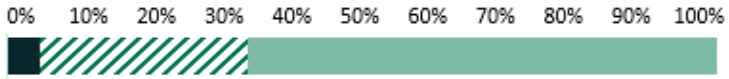
Moxifloxacin (Mfx) — **1% (1/68)** - *4% (1/23)*

Metabolic reaction



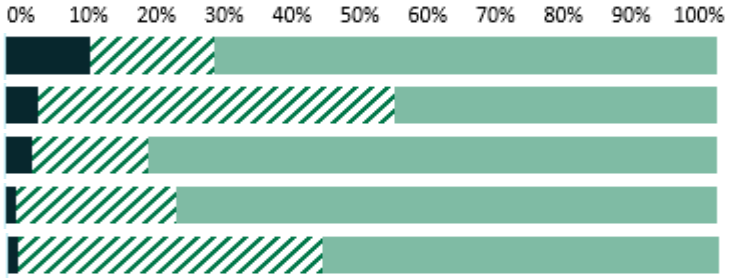
Linezolid (Lzd) — **2% (2/85)** - *8% (2/25)*

Musculoskeletal reaction



Moxifloxacin (Mfx) — **4% (3/68)** - *13% (3/23)*

Neurological reaction



Linezolid (Lzd) — **12% (10/85)** - *40% (10/25)*

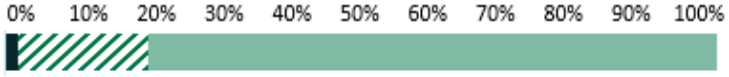
Capreomycin (Cm) — **5% (1/22)** - *8% (1/12)*

Prothionamide (Pto) — **4% (2/55)** - *18% (2/11)*

Cycloserine (Cs) — **1% (1/71)** - *6% (1/17)*

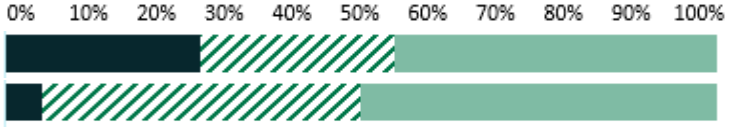
Isoniazid (H) — **1% (1/68)** - *3% (1/30)*

Psychiatric reaction



Prothionamide (Pto) — **2% (1/55)** - *9% (1/11)*

Renal reaction

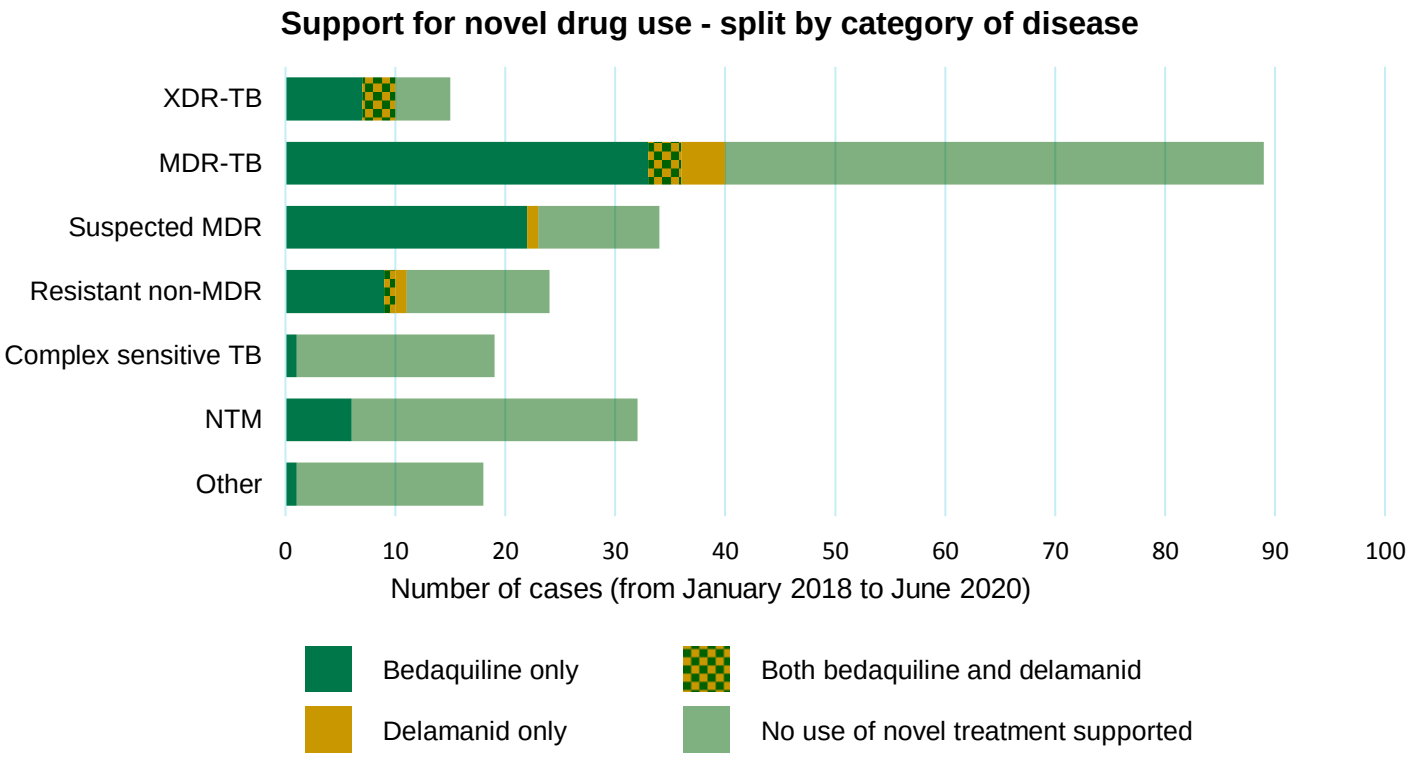


Capreomycin (Cm) — **27% (6/22)** - *50% (6/12)*

Amikacin (Am) — **5% (3/60)** - *10% (3/30)*

Overview 3: 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 within the Clinical Advice Service from each category of disease as reported at entry to the Service (excluding 'Other complex TB', as support to use novel drug therapy was neither requested nor given for any of these cases). Further data analysis is required to determine whether cases reported as suspected MDR-TB at presentation are later confirmed to be so.

Percentage breakdowns are included in the table below. The proportion of cases where the panel of expert CSAs advised the clinician to use one or more novel drug treatments is high (over half – 53% - of cases reported to have XDR, MDR or suspected MDR-TB). Considering the gatekeeping function carried out by 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. Given the change in WHO recommendation, 100% of all new MDR and XDR-TB patients should be prescribed bedaquiline.

	Bedaquiline only	Both bedaquiline and delamanid	Delamanid only	No use of novel treatment supported
XDR-TB	47% (7/15)	20% (3/15)		33% (5/15)
MDR-TB	37% (33/89)	3% (3/89)	4% (4/89)	55% (49/89)
Suspected MDR-TB	65% (22/34)		3% (1/34)	32% (11/34)
Resistant non-MDR	38% (9/24)	4% (1/24)	4% (1/24)	54% (13/24)
Complex sensitive TB	5% (1/19)			95% (18/19)
NTM	19% (6/32)			81% (26/32)
Other	6% (1/18)			94% (17/18)