undergoes identical PK and metabolism in vivo. Dynamic 18F-pretomanid PET/CT imaging was performed in preclinical models to study the biodistribution of 18F-pretomanid. (B) PET signal was quantified in multiple compartments to generate time activity curves (TACs) used to calculate area under the curve (AUC) to plasma (F) suggest drug accumulation due to the long half-life. (G) While 18F-pretomanid PET/CT show vascular leakage and neuroinflammation in the rabbit model, 18F-pretomanid is heterogeneous, and reduced at the lesion site (indicated by white arrow). (H) Quantification of the PET signal shows variability within the same animal. Data are represented as median ± interquartile range, n=3-5 group.

Figure 2. Spatial heterogeneity of 18F-Pretomanid penetration and vascular supply to pulmonary TB lesions.

(A) Experimental timeline used to assess the penetration of pretomanid into infected mouse brain before and during treatment with antimicrobials bedaquiline (B), pretomanid (Pa), and linezolid (L), and corticosteroid dexamethasone (D). (B) Representative three-dimensional MIP of 18F-pretomanid PET/CT in the CNS-TB model, 10 min post-injection, and transverse section showing high and heterogeneous brain uptake. (C) High-resolution autoradiography was pretomanid confirmed heterogeneous penetration of 18F-pretomanid into infected brain lesions in the mouse. (D) 8F-pretomanid AUC ratios of tissue to plasma in mouse brain before (day 0) and two weeks into treatment show a reduction in penetration at week 2. (E) Pretomanid concentration in brain at days 0 and 2 h after injection. (F) Pretomanid concentration in brain at days 0 and 2 h after injection. (G) Pretomanid concentration in brain at days 0 and 2 h after injection. (H) Pretomanid concentration in brain at days 0 and 2 h after injection.

Results.

18F-Pretomanid PET provided detailed concentration-time profiles in infected tissues demonstrating excellent lung and brain tissue penetration (AUC ratio to plasma > 1) in both animal species, which was spatially compartmentalized, likely due to differential vascular supply (18F-pretomanid PET) (Figure 2). Brain lesions (identified by 18F-FDG PET) demonstrated localized lacunae on 18F-pretomanid PET. Autoradiography and mass spectrometry corroborated the imaging findings. The efficacy of the BPaL regimen in TB meningitis was substantially lower than standard TB treatment (Figure 3), likely due to restricted penetration of bedaquiline and linezolid into the brain parenchyma.

Figure 3. Exposure levels of 18/19F-pretomanid in models of TB meningitis.

(A) A novel synthetic was devised to obtain 18F-pretomanid, which is chemically identical to pretomanid. (B) Maximum intensity projection (MIP) of 18F-Pretomanid PET/CT in Mtb-infected mice over 3 hrs shows hepatobiliary and renal excretion, high uptake into brown fat, brain, and lungs. (C) Resection of infected lungs 30 minutes post intravenous administration of 18F-pretomanid shows heterogenous distribution of 18F-pretomanid into the lungs visible by high resolution autoradiography. Areas of pneumonia are identifiable by hematoxylin and eosin (H&E) staining of the same tissue section used for autoradiography. (D) Time-activity curves of 18F-Pretomanid in infected mouse brain before and during treatment with antimicrobials bedaquiline (B), pretomanid (Pa), and linezolid (L), and corticosteroid dexamethasone (D). (E) Mass spectrometry analysis was performed to confirm the brain penetration of 18F-pretomanid, 18F-linezolid, and 18F-pretomanid following oral administration. (F) PET signal shows variability within the same animal. Data are represented as median ± interquartile range, n=3-5 group.

1412. Clinical Epidemiology and Characteristics of Pulmonary Nontuberculous Mycobacterial Isolates from a Large Academic Military Treatment Facility Mary B. Ford, MD; Jason Okulicz, MD; Jesse Salinas, n/a; John Kiley, MD; Brooke Medical Center, JBSA Fort Sam Houston, TX, San Antonio, Texas

Methods. BACM pulmonary NTM isolates from 2012-2020 were included. Corresponding electronic health records were reviewed for epidemiologic, microbiologic, and clinical data. Pulmonary NTM infection (pNTMi) was defined using 2020 NTM guidelines and patients were divided into 2 groups based on whether guideline criteria for pNTMi were met. Demographic, microbiologic, and clinical characteristics were compared between groups.

Results. A total of 813 isolates from 225 patients were analyzed (median 2 [IQR 1-4] isolates per patient). Approximately half (49.7%) were female with a median age of 71 years (IQR 62-79, Table 1), and the majority were current or former smokers (57.3%). Compared to those not meeting criteria (n=116; 51.6%), pNTMi patients (n=109; 48.4%) more commonly had bronchiectasis (47.7% vs 27.6; p=0.002) but were less likely to have solid organ malignancy (11.9% vs 23.3%; p=0.036). A higher proportion of pNTMi patients were female (58% vs 42%; p=0.005) and had lower median Body Mass Index (BMI, 22.6 vs 25.1; p=0.001). M. avium complex (MAC) was more common among pNTMi patients (75.2% vs 35.3%; p=0.001). In contrast, M. simulans and M. gordoniae were more likely to be isolated from those not meeting criteria (35.2% vs 16.8%; p=0.003 and 3.6% vs 1.8%; p=0.001, respectively). Among pNTMi patients, 60 (55%) were offered therapy and were more likely to be younger (70 [IQR 63-76] vs 73 [IQR 65-82] years; p=0.049), have chronic obstructive pulmonary disease (COPD; 51.7% vs 24.5%; p=0.006) and MAC (88.3% vs 59.2%; p=0.001) compared to untreated patients (Table 2).
Approximately half of pNTM isolates were observed in patients who did not meet criteria for pNTMi diagnosis. Female patients, lower BMI, bronchiectasis, or MAC isolation were more likely to meet pNTMi criteria. Management of pNTMi remains a challenge, with younger patients with COPD and MAC more likely to receive treatment.

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1413. Effect of Automated Identification of Antimicrobial Stewardship Opportunities for Urinary Tract Infections
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Background. The treatment of asymptomatic bacteriuria (ASB) does not improve clinical outcomes in most patients and may be associated with an increased risk of adverse events such as Clostridioides difficile infection. A best practice alert (BPA) was created to identify patients with possible ASB for antimicrobial stewardship (AS) review. We aimed to determine whether automated identification of ASB improved the timing of stewardship intervention.

Methods. An electronic health record BPA message to inpatient AS pharmacists was activated on 01/19/2021. The BPA identified inpatients with a new antibiotic order with an associated genitourinary indication and a preceding urinalysis with 0 to 5 WBC/hpf. BPAs were reviewed by an AS pharmacist during weekdays and normal business hours. We retrospectively evaluated the impact of the BPA on time from order to stewardship intervention between a cohort of pre-BPA (01/2020 to 12/2020) and post-BPA (01/2020 to 04/10/2021) patients. Included patients met the BPA criteria and had an AS intervention within 7 days of the antibiotic order. We specified interventions that were UTI-related. The median time from antibiotic order entry to any AS intervention was compared pre- to post-BPA using the Mann Whitney U test. Rates of UTI-related interventions were compared with Fisher's Exact test.

Results. 327 antibiotic orders met BPA criteria and were analyzed: 245 and 82 in the pre- and post-BPA group, respectively. Groups had similar baseline characteristics (Table 1). A total of 33 (27 UTI-related) pre-BPA group and 24 (17 UTI-related) post-BPA group interventions were documented by the AS team. The median time to any intervention was 28 hours (IQR 18-64.5) in the pre-BPA group compared to 3.5 hours (IQR 2.5-10.5) in the post-BPA group (p = 0.03, Figure). The pre-BPA group had a lower rate of UTI-related interventions compared to the post-BPA group (11.0% vs 20.7%, p = 0.04).

Conclusion. Automated identification of antibiotics targeting UTI with urinalysis showing absence of pyuria reduced the time to stewardship intervention and increased rate of UTI-specific interventions. The use of clinical decision support may aid in efficiency of AS review and syndrome-targeted AS impact.

Table 1: Baseline Characteristics

| Characteristics | Eligible Pre-BPA (n = 245) | Eligible Post-BPA (n = 82) |
|-----------------|--------------------------|--------------------------|
| Median age, years (IQR) | 64 (45-74) | 58 (39-72) |
| Sex, male (%) | 101 (41.9) | 32 (39) |
| Race | | |
| Caucasian | 141 (55.9) | 49 (59.8) |
| African American | 79 (32.2) | 23 (28) |
| Other | 25 (10.2) | 10 (12.2) |
| eGFR within 48 hours | 107 (80.4) | 75 (95.3) |
| Median gBS (IQR) | 71 (49-93) mL/min/1.73m² | 75 (50-92.5) mL/min/1.73m² |
| Pregnant | 3 (1.2) | 0 (0) |
| WBC within 48 hours | 232 (162.3) | 80 (95.6) |
| Median Serum WBC (IQR) | 8.9 (6.5-13) x10³/µL | 9.7 (7.5-11.3) x10³/µL |
| ANC ≥ 1000 | 3 (1.2) | 2 (5) |
| Urinary catheter | 69 (23.7) | 15 (18.3) |
| Urinalysis | | |
| Positive nitrite | 66 (26.9) | 26 (31.7) |
| Urine culture in preceding 7 days | 237 (92.6) | 74 (89.3) |
| No growth | 35 (14.5) | 13 (17.0) |
| Mixed flora | 73 (33) | 16 (19.5) |
| < 10,000 cfu/ml, organisms | 185 (72.8) | 75 (92.0) |
| Organism(s) identified | 116 (42.4) | 27 (32.9) |
| Urine culture organism | 116 (46.0) | 27 (32.9) |
| Enterococci spp. | 80 (31.9) | 15 (18.5) |
| Enterococcus spp. | 7 (14.3) | 7 (25.9) |
| Pseudomonas aeruginosa | 4 (3.4) | 0 (0) |
| Other | 10 (4.4) | 5 (6.1) |

1 Data reported as n (%) or median (IQR)
2 eGFR: estimated glomerular filtration rate; WBC: white blood cell; ANC: absolute neutrophil count

Figure: Time-to-intervention among patients with UTI antibiotic order indication, absence of pyuria, and stewardship intervention

Conclusion. Automated identification of antibiotics targeting UTI with urinalysis showing absence of pyuria reduced the time to stewardship intervention and increased rate of UTI-specific interventions. The use of clinical decision support may aid in efficiency of AS review and syndrome-targeted AS impact.