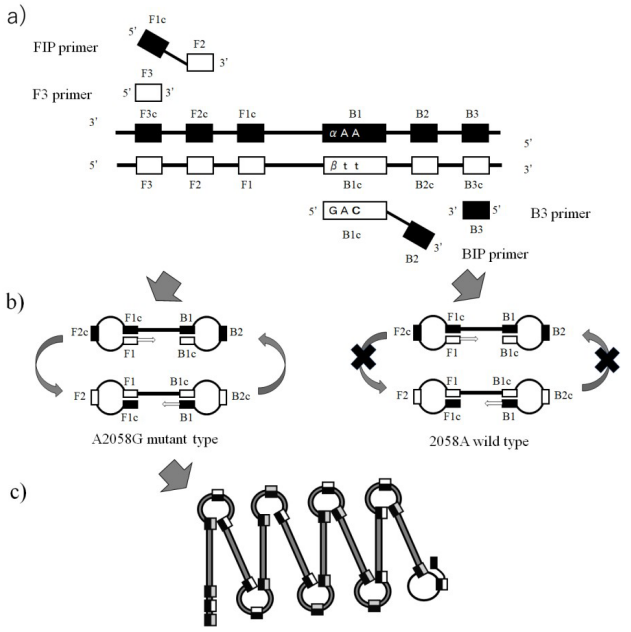
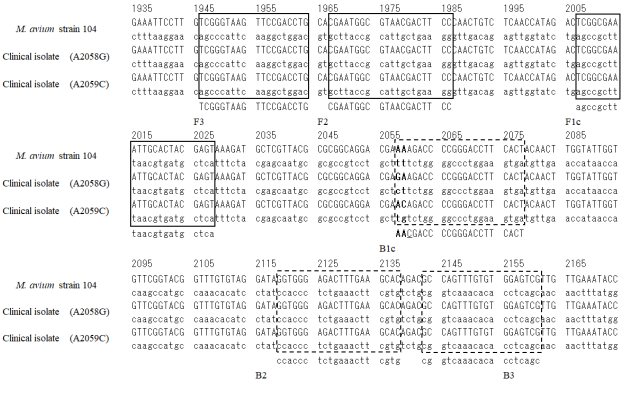
Figure 1. The designs of CLR resistance A2058G mutant-type mismatch primers used for the ARMS-LAMP assay. a) A strand-displacing DNA polymerase extends the DNA from FIP while separating from the DNA chain. The primer F3 binds to its complementary region on the DNA to displace the newly synthesized DNA. An analogous reaction is performed by BIP and B3. α (α = A, wild type; G, A2058G) and β (β = A, wild type; C, A2058G) are indicated by the point mutation at position 2058 of the 23S rRNA gene. The bold area indicates the mismatched base C (cytosine). b) The synthesized DNA self-anneals because of the complementary region at both ends and forms 'dumbbell' structures. c) After repeated rounds, a complementary region on the same chain is amplified.



Methods: Primers for ARMS-LAMP were designed using PrimerExplorerV5 software based on the nucleotide sequence data for 23S rRNA in *M. avium* strain 104 (Figure 2). Using the minimum inhibitory concentration of CLR, drug susceptibility was determined for 18 clinical *M. avium* isolates. Of these, eight CLR-susceptible and 10 CLR-resistant strains were analyzed by sequencing the 23S rRNA gene and ARMS-LAMP.

Figure 2. Alignment of the nucleotide sequences including the domain V region of 23S rRNA at the macrolide binding site. The constructed LAMP primer sets are shown in solid boxes (forward primers, F1-3) and dashed boxes (backward primers, B1-3). The bold area indicates the point mutation at position 2058 or 2059 of the 23S rRNA gene.



Results: Sequence analysis revealed that all eight CLR-sensitive strains tested were wild type, whereas all 10 CLR-resistant strains were mutants. Using ARMS-LAMP, no amplification with the mutant-type mismatch primer sets (MTPS) was observed in the eight wild-type strains, but amplification was observed with MTPS in the 10 mutant strains (Table 1).

Table 1. MICs of CLR and results of ARMS–LAMP using Mycobacterium avium isolates.

Strains	Total number	MIC (μg/mL)	ARMS-LAMP
Reference strain			
Mycobacterium avium 104	1	0.25	-
Clinical isolates			
CLR susceptible strains	8	< 8	-
CLR resistant strains	10	>32	+

CLR, clarithromycin. MIC, minimum inhibitory concentration. +, positive. -, negative. ARMS-LAMP, amplification refractory mutation system -loop-mediated isothermal amplification.

Conclusion: The developed rapid detection method for the CLR resistance gene using ARMS-LAMP can determine drug resistance in a few hours without the need for special equipment. ARMS-LAMP may be a new clinically beneficial POCT technology for examination that is novel and extremely practical.

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1655. Extrapulmonary Tuberculosis in a Large Healthcare System

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. The US has seen a rise in the proportion of patients with extrapulmonary tuberculosis (TB) even though the yearly incidence of new TB cases has been in decline. The purpose of this study was to analyze incidence of extrapulmonary TB at Atrium Health, a large non-profit health system in the Southeastern US.

Methods. Retrospective chart review of 94 adult patients with culture confirmed extrapulmonary TB between 2008-2019. Individuals younger than 18 years were excluded from analysis. The primary objective was to examine incidence of extrapulmonary TB and compare it to that reported in the literature. Secondary objectives included determination of sites of extrapulmonary disease and associated patient characteristics including HIV status, race, ethnicity, and birthplace.

Results. 237 patients were identified as having confirmed TB infection from 2008-2019 in a retrospective analysis within the Atrium Health System. 94 (40%) were found to have extrapulmonary disease; 42 (45%) with concomitant pulmonary disease. The patients were 55% male, 40% African American, 21% Hispanic or Latino, and 51% US-born. Median age was 44 years (range 20-62). The most common sites of extrapulmonary TB were lymphatic (35%), pleural (24%), GI/Peritoneal (12%), CNS (10%), and Bone/Joint (10%). Lymphatic involvement was 40% cervical, 19% intrathoracic, and 16% axillary. 66% of skeletal disease was vertebral. Other sites included GU, pericardial, skin, and disseminated disease (5%). 37% were HIV positive, 18% with unknown HIV status as they were never tested. Information regarding patient's race, ethnicity, and birthplace were unknown for 2 patients. The percentage of extrapulmonary cases were 29% in 2008, 39% in 2012, 38% in 2016, and 49% in 2019.

Conclusion. Lymphatic and pleural involvement were the most common extrapulmonary sites. Of those tested, 37% were HIV positive but there was a significant portion never tested showing a need for increased testing. The proportion of extrapulmonary TB cases since 2008 is higher at 40% compared to the 31% reported in the United States. There has been a rise in the proportion of extrapulmonary TB within our healthcare system and deserves further analysis.

Disclosures. **All Authors**: No reported disclosures

1656. Factors associated with low TB preventative therapy prescription rates among healthcare workers in rural South Africa

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Despite South Africa's initial successful rollout of tuberculosis preventative therapy (TPT) to reduce tuberculosis (TB) incidence among HIV-infected

patients, recent data suggest prescription rates have decreased. This study aimed to identify associations with low prescription rates among healthcare workers (HCWs) in rural South Africa.

Methods. A cross-sectional survey was administered Nov-Dec 2019 to HCWs at a 350 bed rural district hospital and 14 primary care clinics (PCCs) in the Msinga sub-district, South Africa to obtain self-reported data on prescription rates as well as knowledge, attitudes, practices, and beliefs regarding isoniazid preventive therapy, the current TPT regimen. HCWs included professional nurses, staff nurses, counselors, and medical officers. Survey questions were consolidated into scores using exploratory factor analysis. Univariate and multivariate associations with low prescription rates, defined as < 50% of eligible patients, were determined for prescribers.

Results. Among 160 participants, the median (+ IQR) age was 39 (+13) years, 76% were women, 78% worked at a PCC, and 35% were prescribers, including professional nurses (82%) and medical officers (19%). The median (+ IQR) years as a HCW and managing patients living with HIV (PLH) among prescribers was 14 (+ 15.5) and 10 (+ 11.5) years, respectively. Compared to prescribers, non-prescribers reported more stigma (71% v. 54%; p=0.04) and placed less priority on prevention compared to treatment (32% v. 58%; p< 0.01). Among prescribers (n=54), univariate analysis identified that patient nondisclosure (OR 4.17 95% CI 1.23-14.14; p=0.02) was associated with low TPT prescription rates. Poor self-reported knowledge also trended towards significance (OR 5.23 95% CI 0.85-32.08; p=0.07). After multivariate analysis, only perceived patient nondisclosure was significantly associated with low prescription TPT rates (aOR 4.17 95% CI 1.23-14.14; p=0.02).

Conclusion. HCWs who believed their patients had not disclosed that they were taking TPT were significantly less likely to prescribe it to their patients. Strengthening HCW training about indications for and mortality benefit of TPT as well as stigma reduction is critical to enhancing TPT implementation.

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1657. Musculoskeletal Tuberculosis in a Large Healthcare System

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Musculoskeletal tuberculosis (TB) is an important and elusive manifestation of extrapulmonary TB. This purpose of this study was to examine incidence and associated co-morbidities of confirmed cases of musculoskeletal TB at Atrium Health, a large non-profit health system in the Southeastern United States.

Methods. Retrospective case series of 12 adult patients with confirmed musculoskeletal TB between 2008-2019. Individuals younger than 18 years were excluded. The primary objective was to compare local incidence of musculoskeletal TB with that reported in the literature. Secondary objectives included analysis of patient co-morbidities for their correlation with the development of musculoskeletal manifestations of TB and requirement of surgical correction for underlying deformities from TB infection.

Results. 237 patients were identified with confirmed TB infection from 2008-2019 in a retrospective cohort within the Atrium Health System. Of 237 patients, 94 (40%) had extrapulmonary disease and 12 (5%) had musculoskeletal manifestations defined as involvement of bone, joint space, or muscle and were included in this analysis. Six (50%) of the 12 patients were foreign born individuals who immigrated to the US. Three (33%) had concomitant pulmonary disease. Vertebral involvement (8, 66%) was most common and 1 (8%) patient noted to have infected total knee arthroplasty. Other sites included wrist, sternum, ribs and pelvis. Co-morbidities evaluated included HIV status 0%, diabetes (2, 17%), immunosuppressive medications (1, 8%), ESRD 0%, and rheumatologic disease 0%. Surgical intervention was necessary in 4 (33%) patients for both diagnostic and therapeutic interventions.

Conclusion. Of those tested for HIV 100% were negative but only 50% were tested showing a need for improved HIV testing. Very few had other co-morbid conditions including diabetes, use of immunosuppressive medications, ESRD status, or rheumatologic disease. Surgical intervention was needed in 33% of patients with musculoskeletal TB including several with a preoperative suspected diagnosis of malignancy. In this retrospective case series, the incidence of musculoskeletal TB was 5% in comparison to the 2-3% reported consistently in the US.

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1658. Particularities Of Pulmonary Tuberculosis Among Children

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. The diagnosis of pulmonary tuberculosis (PTB) among children remains challenging due to the non-specific clinical symptoms, laboratory features and the difficulty of sampling for microbiological investigations. We aimed to study clinical, therapeutic and evolutionary features of PTB among children.

Methods. We conducted a retrospective study including all children aged ≤ 18 years diagnosed with PTB between 1995 and 2016.

Results. We encountered 67 children with PTB, among whom 37 (55.2%) were female. The median age was 15 years [1-18years]. According to residency, 36 patients came from rural area (53.7%). We noted 7 cases (10.4%) of miliary tuberculosis (TB). Three cases of pleural TB (4.5%), one case of lymph node TB (1.5%) and one case of neuromeningeal TB were associated to PTB. Induced sputum or gastric aspirate were positive for *Mycobacterium tuberculosis* in 67.9% of the cases. Serologic tests for human immunodeficiency virus was positive in one case (1.5%). The mean duration of antitubercular therapy was 8 ±2 months. The treatment regimen was based on a quadritherapy for the first 2 months, followed by a bitherapy for the rest of the period. Fixed dose drug combinations were prescribed in 17 cases (25.3%). The disease evolution was favourable in 65 cases (97%). Two patients were dead (3%). There were no relapsing cases.

Conclusion. Prompt diagnosis and treatment of PTB among children improve the prognosis. Screening for PTB among children exposed to adult tuberculosis is crucial in order to prevent the disease.

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1659. Pharmacokinetics/pharmacodynamics of the Novel Gyrase Inhibitor SPR719/SPR720 and Clinical Dose Selection to Treat Pulmonary Mycobacterium avium-complex Disease

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Current therapy for pulmonary *Mycobacterium avium-complex* [*MAC*] disease achieves poor sustained sputum conversion rates and is poorly tolerated. SPR719, the active metabolite of SPR720, a novel gyrase inhibitor, has demonstrated low MICs against MAC. SPR720 is being developed as an oral therapy for use in combination with other antibiotics for the treatment of patients with pulmonary disease due to infection with MAC. Our objective was identify SPR719 pharmacokinetic/pharmacodynamic [PK/PD] parameters and optimal SPR720 dose for treatment of pulmonary MAC.

Methods. SPR719 was administered once daily for 28 days using a simulated human half-life of 3.3 hours in the hollow fiber system model of pulmonary intracellular MAC [HFS-MAC]. Bacterial burden, including for SPR719-resistant subpopulations, and drug concentrations, were measured via repetitive sampling of HFS-MAC units. A separate dose fractionation study in the HFS-MAC was used to identify the PK/PD index linked to effect. MAC burden versus SPR719 exposure was modeled using the inhibitory sigmoid maximal effect [E_{max}] model and resistance using the "antibiotic resistance arrow of time" model. Finally, we performed Monte Carlo Experiments to identify the optimal clinical dose of SPR720 monotherapy.

Results. The median HFS-MAC intracellular-to-extracellular SPR719 $AUC_{0\text{-}24}$ ratio was 2300:1. The PK/PD parameter best linked to microbial kill was determined to be $AUC_{0\text{-}24}$/MIC. SPR719 E_{max} was -1.5 $\log_{10}$ cfu/mL compared to day 0; 1.0 $\log_{10}$ cfu/mL reduction and acquired-resistance suppression were achieved by an $AUC_{0\text{-}24}$/MIC of 2.0 and 11, respectively. SPR720 1,000 mg/day was predicted to achieve 1.0 $\log_{10}$ cfu/mL kill in 95%, and resistance suppression in 43%, of 10,000 simulated subjects.

Conclusion. SPR720 monotherapy is predicted to achieve exposures associated with bactericidal effect against pulmonary MAC in 95% of patients at doses that have recently been established to be safe and well tolerated. These data support the continued development of SPR720 for the treatment of pulmonary MAC.

Disclosures. Nicole Cotroneo, Spero Therapeutics (Employee) David Melnick, MD, Spero Therapeutics (Employee)Spero Therapeutics (Employee) Troy Lister, PhD, Spero Therapeutics (Employee) Suzanne Stokes, PhD, Spero Therapeutics (Employee, Shareholder) Tawanda Gumbo, MD, Praedicare Inc (Employee, Shareholder)

1660. Prevalence and Predictors of Anxiety and Depression among Leprosy Patients using the Hospital Anxiety and Depression Scale-Pilipino Score in a Tertiary Hospital

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. This study was prompted by significant reports of anxiety and depression among people with skin disorders in clinical settings and primarily focuses on leprosy patients.

Methods. This is a cross-sectional descriptive study conducted at Dr Jose N. Rodriguez Memorial Hospital located at Tala, Caloocan City, Philippines. All patients admitted at the Custodial ward and seen at the outpatient during the study period will be included using convenience sampling. The prevalence of anxiety and depression was determined by a score of 8 points or higher on the HADS-P. Logistic regression analysis was utilized to determine the relationship between the socio demographic data and clinical variables with anxiety and depression. Odds ratio were calculated and P-value < 0.05 were considered as statistically significant.

Results. Among the 150 Leprosy patients included in the study with a HADS-P score of 8 and above per category showed that 86 (57.33%) of the respondents have anxiety and 37 (24.67%) have depression. Running a logistic model that predicts a person having an anxiety, having hypertension as well as having a minor disability were proven to be significant with p-value 0.02 and 0.09 respectively. An odds ratio of 3.01 denotes that a person with hypertension is twice (2.01) as likely to have anxiety than a person with no comorbidities. Running a logistic model that predicts a person having