## **Research Themes and Aims**

There are 7 research themes within CoSTAR-HS:

- 1. Primary Care Antimicrobial Stewardship (PC-AMS) Optimising antibiotic prescribing in primary care
  - To study the prevalence of antibiotic-resistant bacteria causing common infections (such as UTIs and soft tissue infections (STIs)) that are managed in the primary care setting, establishing routine surveillance and isolate collection for these bacteria for subsequent analysis. These data and isolates will generate new research hypotheses and pave the way for further collaborations with partner institutions. After cross-validation with data from other primary public healthcare institutions and international antimicrobial guidelines, these data can also be used to develop relevant and time-sensitive local guidelines.
  - To program a new in-built function within our IT systems to collect and analyse data on the prevalence of infections, indications, and appropriateness of antibiotic prescriptions, as well as the prescribing habits of primary care physicians. These data will be used to understand physicians' knowledge, attitudes, practices, perceptions, and barriers that will inform subsequent interventions to optimise antimicrobial stewardship.
  - To develop educational and clinical interventions to strengthen the rational prescription of antibiotics in primary care. Outcomes of interventions will be assessed. Interventions implemented at NUP may then be similarly and subsequently implemented in private general practices and other primary public healthcare institutions.

#### 2. Health systems, policies, and economics in AMR control

- To identify and evaluate policies, programmes and structures that address AMR both locally and in the region, using an adapted governance framework.
- To examine the motivations, social constructs, contextual drivers, and power relations of policy actors that influence behaviours and decision-making processes in developing policies for AMR, specifically in relation to the AMR control in primary care and hospitals.
- To assess the health systems barriers comprehensively and facilitators (including but not limited to surveillance, stewardship and infection prevention and control) to address AMR in the community.
- To develop strategies and tools for working with policymakers to implement AMR control policies in human health effectively.

## 3. Population CPE Epidemiology To Guide Infection Prevention

- To determine the ongoing sources of endemic XDR-GNB transmission following the intensification of CPE infection prevention measures: the next 5 years (2016 to 2020).
- To determine the impact of Covid-19 on XDR-GNB population transmission.

## 4. Built environment: The Achilles heel of MDRO control in healthcare facilities

- To explore environmental microbiome and bacterial genomics to identify factors associated with persistence and onward transmission of MDROs.
- To improve existing infection prevention and control (IPC) strategies and explore novel technologies to prevent environment-mediated infections with MDROs.

# 5. Detecting Antibiotic Resistance and Bacterial Persistence to Identify Innovative Treatment Strategies against XDR-GNB

- To employ a systems biology approach integrating multi-omics (genomics, transcriptomics and proteomics) data to construct network models to describe antibiotic resistance and bacterial persistence.
- To push the boundaries of pharmacokinetic/pharmacodynamic (PK/PD) translational research by improving our current in vitro combination testing platform to improve turnaround time and identify novel diagnostics and innovative treatment strategies.

#### 6. Benchtop-to-bedside and beyond: Incorporating analytics and augmented intelligence (AI) strategies for the treatment of infections caused by multi-drug resistant organisms (MDROs)

- To leverage on existing health information technology (IT) to build an XDR-GNB data lake that includes clinical and outcome data of patients infected by XDR-GNB, phenotypic and genomic data of the infecting XDR-GNB, as well as results of more extensive testing of the isolates (such as proteomics and MCBT data) where available. We currently have more than 6,000 inpatient datasets with their archived XDR-GNB in our registry, growing at approximately 1,200 per year in SGH.
- To develop prediction models and machine learning systems with our XDR-GNB data lake in the exploratory development of a patient-centric, individualised-management approach that delivers the "right drug at the right dose for the right patient at the right time" for both empiric and targeted therapies against respiratory tract infection including pneumonia, and urinary tract infection (which constituted the top 2 highest infectious diseases burden in Singapore).

#### 7. Innovative Clinical Trials

- To develop novel clinical trial methodologies to improve the efficiency of trial conduct, maximise data utility and accelerate evidence synthesis.
- To expand local capacity in trial development, implementation and support and establish regional and industrial partnerships to build rapid trial pipelines.