

A Multicenter Prospective Registry to Standardize and Evaluate Personalized Bacteriophage Therapy in Difficult-to-Treat Infections

From PHAGEFORCE to EPHICACI: Scaling Personalized Phage Therapy Across Belgium

Louise Sykora^{1,2}, Laura Bessems^{1,2}, Saartje Uyttebroek³, David Devolder⁴, Paul De Munter^{5,6}, Yves Debaveye⁷, Melissa Depypere^{8,9}, Liesbet Henckaerts¹⁰, Isabel Spriet^{4,11}, Natalie Lorent^{12,17}, Laura Van Gerven^{3,13,14}, An Van Laethem¹⁵, Lieven Dupont^{16,17}, Jean-Paul Pirnay¹⁸, Maya Merabishvili¹⁸, Pieter-Jan Ceysens¹⁹, Jolien Onsea^{1,2} and Willem-Jan Metsemakers^{1,2}, EPHICACI Consortium

¹Department of Development and Regeneration, KU Leuven, Leuven, Belgium, ²Department of Trauma Surgery, University Hospitals Leuven, Leuven, Belgium, ³Department of Otorhinolaryngology, University Hospitals Leuven, Leuven, Belgium, ⁴Pharmacy Department, University Hospitals Leuven, Leuven, Belgium, ⁵Laboratory for Clinical Infectious and Inflammatory Disorders, Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium, ⁶Department of Internal Medicine, University Hospitals Leuven, Leuven, Belgium, ⁷Department of Intensive Care Medicine, University Hospitals Leuven, Leuven, Belgium, ⁸Department of Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium, ⁹Laboratory of Clinical Microbiology, Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium, ¹⁰Department of General Internal Medicine, University Hospitals Leuven, Leuven, Belgium, ¹¹Department of Pharmaceutical and Pharmacological Sciences, Clinical Pharmacology and Pharmacotherapy, KU Leuven, Leuven, Belgium, ¹²Department of Respiratory Diseases, University Hospitals Leuven, Leuven, Belgium, ¹³Department of Neurosciences, Experimental Otorhinolaryngology, Rhinology Research, KU Leuven, Leuven, Belgium, ¹⁴Department of Microbiology, Immunology and Transplantation, Allergy and Clinical Immunology Research Group, KU Leuven, Leuven, Belgium, ¹⁵Department of Dermatology, University Hospitals Leuven, Leuven, Belgium, ¹⁶Department of Pneumology, University Hospitals Leuven, Leuven, Belgium, ¹⁷Department of Chronic Diseases and Metabolism, laboratory of Respiratory Diseases and Thoracic Surgery (BREATHE), KU Leuven, Leuven, Belgium, ¹⁸Laboratory for Molecular and Cellular Technology, Queen Astrid Military Hospital, Brussels, Belgium, ¹⁹Sciensano, Service of Bacterial Diseases, Brussels, Belgium

BACKGROUND

Antimicrobial resistance (AMR) increasingly complicates the management of **musculoskeletal infections (MSI)**, where biofilm formation and implant-associated infections often necessitate prolonged antibiotic therapy, repeated surgical interventions, and are associated with frequent treatment failure (1). **Bacteriophage therapy (PT)** has re-emerged as a promising **adjunctive strategy**, given its specificity, ability to target biofilms, and self-amplifying nature (2). However, clinical implementation remains limited by heterogeneous study designs, lack of standardized protocols, and insufficient clinical evidence (2). The monocentric **PHAGEFORCE** registry demonstrated the feasibility of PT across five medical indications, with clinical remission in 9/11 (82%) evaluable MSI patients and no serious adverse reactions (3). **EPHICACI** was developed to overcome its limited scale through a multicenter approach.

STUDY DESIGN

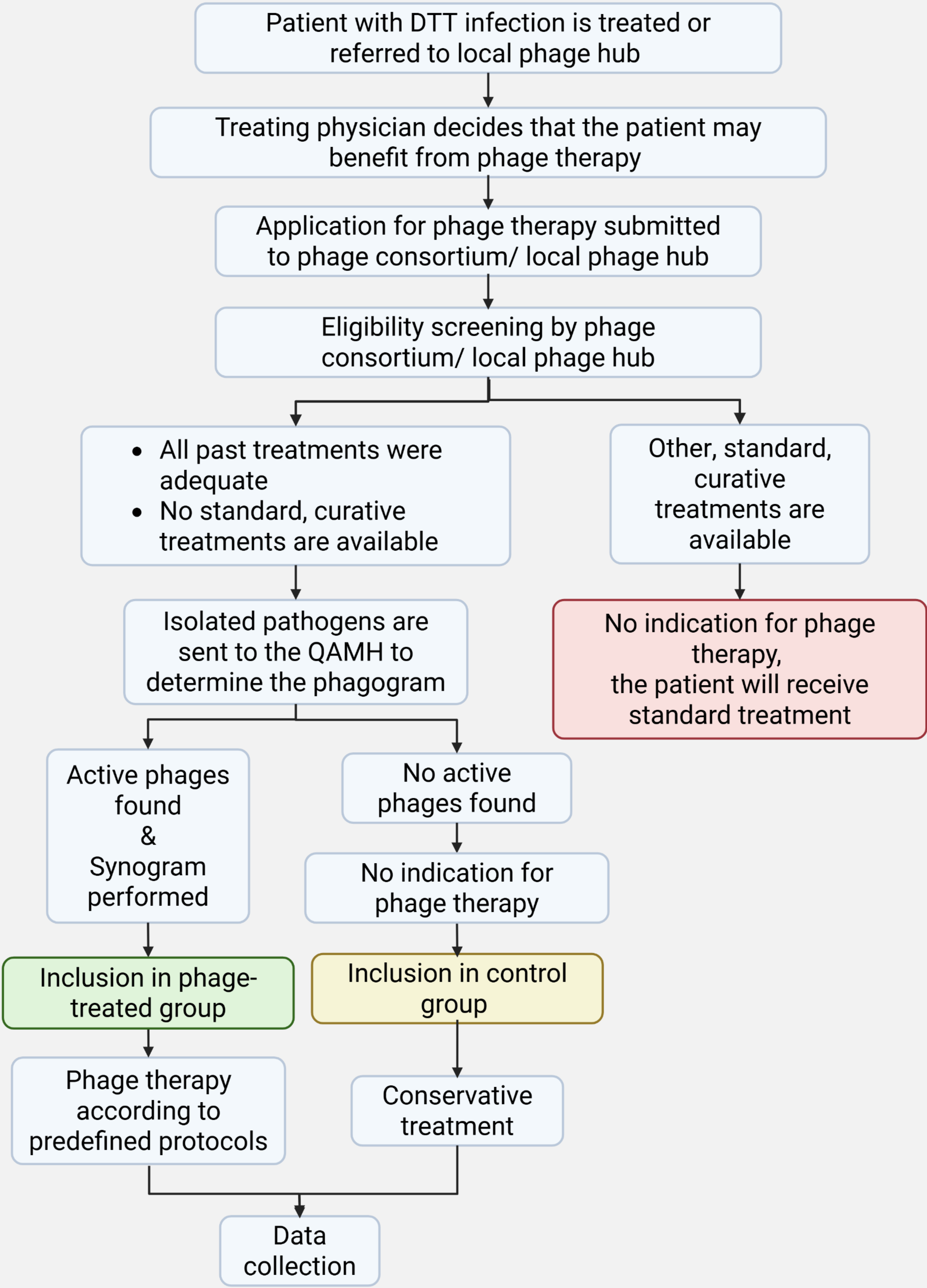
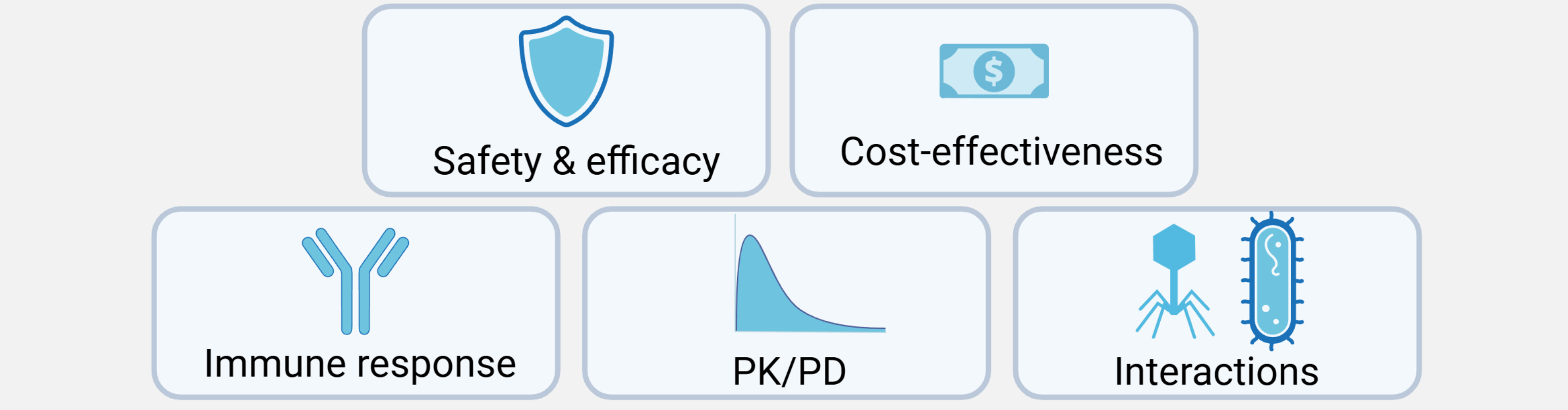


Figure 1. Workflow of the EPHICACI study. Following eligibility screening, bacterial isolates undergo phage susceptibility testing, which determines assignment to the phage-treated or control group.

AIMS



TREATMENT PROTOCOL

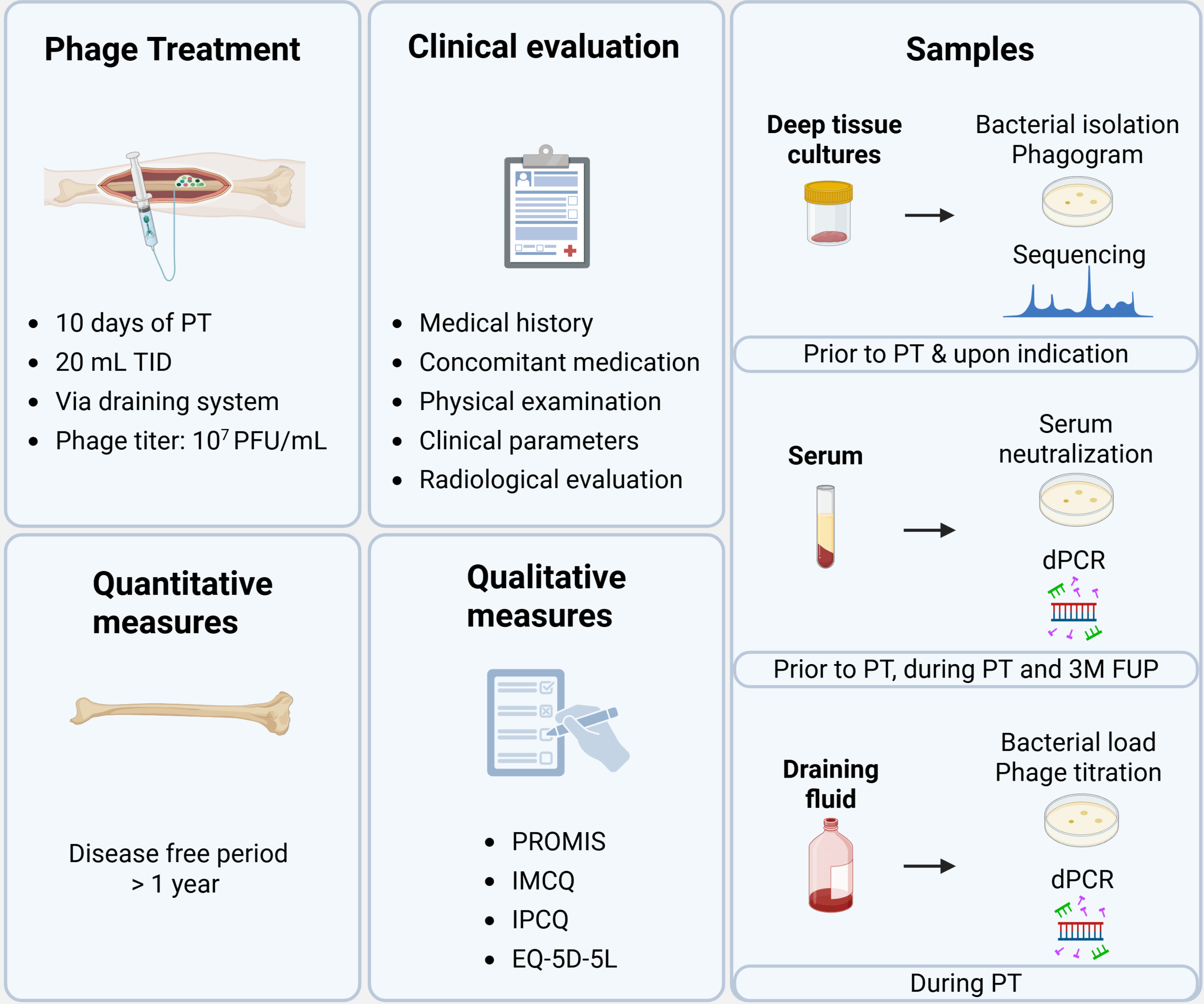
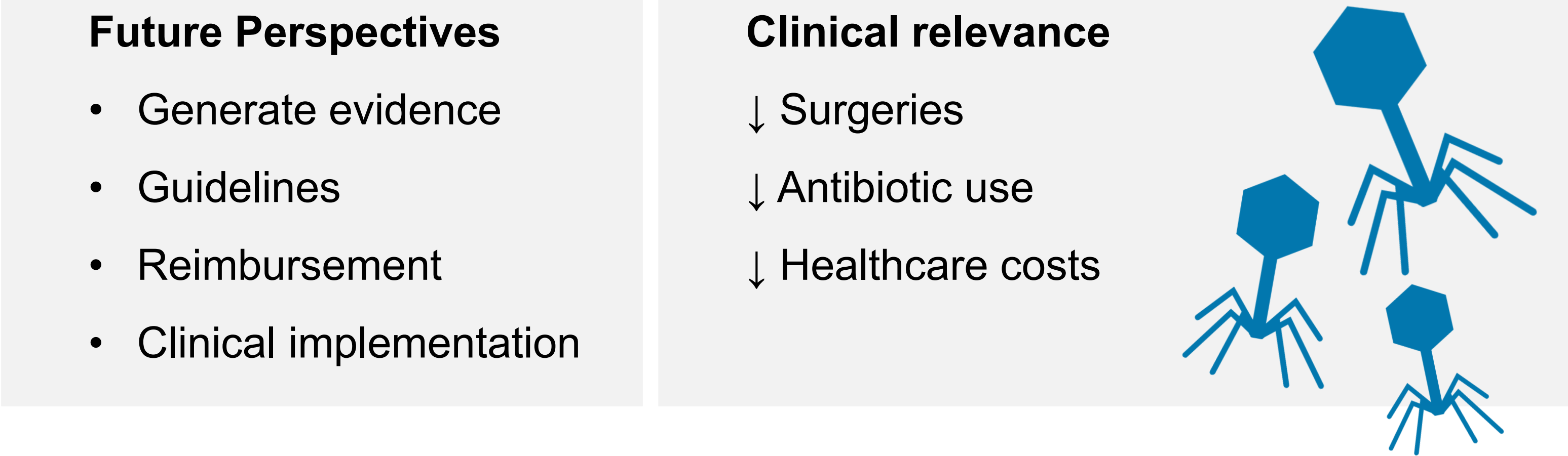


Figure 2. Overview of standardized protocols for phage administration, sampling, and outcome evaluation in MSI patients.



Figure 3. Left: Intraoperative administration of phage therapy via a draining system in MSI. Right: Plaque assay (double agar overlay) used to quantify phage titer.

CLINICAL IMPACT & OUTLOOK



References

1. Metsemakers, et al. (2024). The global burden of fracture-related infection: can we do better? *Lancet Infect Dis*.
2. Uyttebroek, et al. (2022). Safety and efficacy of phage therapy in difficult-to-treat infections: a systematic review. *Lancet Infect Dis*.
3. Onsea, et al. (2019). Bacteriophage Application for Difficult-to-treat Musculoskeletal Infections: Development of a Standardized Multidisciplinary Treatment Protocol. *Viruses*.

Funding

FWO (T002425N)

Collaborators

Military Hospital Queen Astrid & Sciensano

