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Innovations in response-adaptive designs for clinical trials

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Clinical trials have traditionally followed a fixed randomized design, where patients are typically allocated once, at random, and usually equally to various treatments. Such designs provide a clean way of separating out the effects of alternate treatments. Response-adaptive designs, where assignment to treatments evolves dynamically as patient outcomes are observed, are gaining in popularity due to potential for improvements in both cost and efficiency over traditional designs. An ideal adaptive design is one where patients are treated as effectively as possible without sacrificing the potential learning or compromising the integrity of the trial. We propose such a design, termed Jointly Adaptive, which uses forward-looking algorithms to fully exploit learning from multiple patients simultaneously. Compared to the best existing implementable adaptive design that employs a multi-armed bandit framework in a setting where multiple patients arrive sequentially, we show that our proposed design improves health outcomes of patients in the trial, in expectation, by 8.6% under a set of considered scenarios. We also demonstrate our design's effectiveness using data from a recently conducted stent trial, where we demonstrate an improvement of over 37%, in expectation. A consequence of using forward-looking algorithms in the above approach is that the problem size grows exponentially with the number of patients and time periods, making it computationally challenging to solve. To address this, we propose grid-based approximation methods that reduce problem dimensionality and allow for the implementation of adaptive designs to large clinical trials. We use numerical examples to demonstrate the effectiveness of our approach.

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Synergistic effect of biogenic silver-nanoparticles with β lactam Cefotaxime against resistant *Staphylococcus arlettae* AUMC b-163 isolated from T3A pharmaceutical cleanroom, Assiut, Egypt

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The aim of this study was to biosynthesize silver nanoparticles (AgNPs) from *Staphylococcus arlettae* AUMC b-163 isolated from T3A pharmaceutical company clean room, its antimicrobial activity, and the synergistic effect of AgNPs in combination with commonly used antibiotic Cefotaxime sodium against resistant bacteria. The synthesized AgNPs from bacterial were characterized by using UV-VS spectrophotometer analysis, Fourier Transform Infrared Spectroscopy (FTIR), X-ray diffraction (XRD) and Transmission Electron Microscopy (TEM). UV-VS spectrophotometer analysis showed a peak at 420 nm corresponding to the Plasmon absorbance of silver nanoparticles and FTIR analysis showed the potential biomolecule responsible for the reduction of silver. The structural properties of silver nanoparticles were confirmed using XRD technique, while TEM micrographs revealed that the silver nanoparticles are dispersed and aggregated, and mostly having spherical shape within the size range between 8 and 35 nm. The synthesized silver nanoparticles exhibited a varied growth inhibition activity against the tested pathogenic bacteria. A significant increase in area of growth inhibition was observed when a combination of silver nanoparticles and Cefotaxime antibiotics was applied. The current results revealed that the synthesized silver nanoparticles produced by the bacterial strain *Staphylococcus arlettae* AUMC b-163 is promising to be used in medical therapy due to their broad spectrum against some pathogenic bacteria, fungi and resistant tested bacteria.

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