Faculty of Medicine, Cairo University Postgraduate Research Protocol Template
(Please read carefully the provided guidance documents for a comprehensive understanding and proper formulation of your thesis protocol and required forms)

1. Study

a- Proposed Study Title: Feasibility and efficacy of intravenous to oral antimicrobial conversion in hospitalized children.
b- Degree: NA
c- Date of Registration of MSc or MD:

2. Candidate

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4. Scientific committee approval

(Was it scientifically approved by the department?) Yes

Date of approval: 8/12/2025

5. **Background and Rationale:** (Describe the research question and justification for undertaking the study, explaining the aspects of novelty in the study)

The use of antimicrobials in the community contributes to increasing healthcare costs[1,2,3] and increasing microbial resistance[4]. Moreover, the intravenous dosage form has a higher cost than the oral form, a higher risk of nosocomial acquired infections, complications, more workload and duties of healthcare professionals; consequently, there is an increase in the length of hospital stay [5].

The World Health Organization (WHO) defines the rational use of medicines as "patients receive medications appropriate to their clinical needs, in doses that meet their own requirements, for an adequate time, and at the lowest cost to them and their community". In addition, one of the CDC core elements antimicrobial stewardship checklist is "change from intravenous to oral antibiotic therapy in appropriate situations".

Studies conducted in Egypt by Ashour et al. 2022; EzElarab et al. 2019; Hassan et al. 2011; and Shams et al. 2022[6,7,8,9] underscored that a small percentage of antimicrobials were used in the oral dosage form, 1.4%, 13%, 19%, and 3%, respectively. Moreover, Ashour and Hassan mentioned that 53% and 92%, respectively, were inappropriate choices.

Although intravenous medications may have more bioavailability, some oral drugs can reach serum levels comparable to those of the parenteral form. Several antimicrobials have good bioavailability. For instance, quinolones, linezolid, and clindamycin can be used in a sequential or switching intravenous to oral strategy [10,11,12]. Cephalosporin can be used in step down approach or a switching approach. Trimethoprim-sulfamethoxazole can also be used as part of intravenous (IV) to per oral (PO) switch regimens [13]. Antifungals such as voriconazole, itraconazole and fluconazole can be used in a sequential strategy [14]. A clinical pharmacist is one of the core members in antimicrobial stewardship team. Hence, he has a great role in categorizing the candidates for the suitable strategy, selecting the appropriate antimicrobial according to indication and choosing the appropriate dose, determining the appropriate time for administration of oral antimicrobials to avoid food-drug interaction. [15]

This study aims to assess the impact of implementing the IV to PO conversion of antimicrobials in suitable candidates, assess the cost-effectiveness of applying this strategy, and determine whether this strategy reduces nosocomial acquired complications from IV antibiotic delivery. Hence, patients can be discharged from the hospital after tolerance of oral antimicrobial, and assess if it will reduce the length of hospital stay. Moreover, opens a road map for identifying the barriers for effective implementation of intravenous to oral conversion

at hospitals.

6. **Objectives:** (describe specific objectives or hypotheses behind the study)

To determine the efficacy, safety and cost- effectiveness of IV to PO conversion of antimicrobials in hospitalized pediatric patients.

7. **Study Design:**

A- Nature of the study

- Prospective study ■
- Retrospective study ☐

B- Design of the study: (Please insert √ in front of the suitable design)

1-	Case series	
2-	Qualitative	
3-	Survey	
4-	Cross sectional analytic	
5-	Case-control	
6-	Cohort (Longitudinal)	
7-	Randomized Clinical Trial	√
8-	Non-randomized clinical trial	
9-	Animal study	
10-	Cellular study	

- **Other study design:** ☐

  Please describe:

- **Study Methods**

- **Population of study:** (Please provide all details regarding participants including gender, age range and disease conditions. Indicate if this protocol involves children, prisoners, pregnant women or cognitively impaired or mentally disabled subjects. Also

indicate if participants will be divided into groups and mention the characteristics of and number of participants in each group adequately.

This prospective study will be conducted on hospitalized pediatric in both genders who require initiation of IV antimicrobials and are candidates for the IV to PO antimicrobial therapies conversion.

- **Study location:** (Please provide where the study will be conducted and from where study participants will be recruited)

The study will be conducted at the Pediatric ICU at Abo Elreesh Mounira Children's Hospital, Cairo University, after ethical approval.

- **Inclusion criteria:**

- Age more than 1 month to 14 years of both sexes.
- Hospitalized patients with proven infection (community-acquired pneumonia (non-invasive ventilated patients) and uncomplicated urinary tract infection.
- Requiring initiation and continuation of antimicrobials.
- Patient is vitally and hemodynamically stable.
- Afebrile for ≥24 hours
- Tolerate enteral feeds and take medications orally.

- **Exclusion criteria:**

- Patients with GI Disorders (e.g., obstruction, malabsorption, active GI bleeding, nothing by mouth (NPO), Short Gut syndrome, continuous feeds that cannot be held if the antimicrobial agent has a food interaction).
- CNS Disorders: seizure and risk of aspiration.
- Hemodynamic instability: hypotension or shock.
- Patients refusing oral medication.
- Febrile neutropenia < 1000 cells/mm^3 or functional asplenia.
- Severe infection or deep-seated infection (e.g., meningitis, endocarditis, deep abscess, initiation of treatment in bone and joint infections, infected prosthesis)

- Surgical prophylaxis patients.

Withdrawal criteria : Participants will be withdrawn if any of the following occur:

- Clinical deterioration requiring escalation of care
- Inability to tolerate oral medication
- Development of severe complications or new infection.

All withdrawn participants will continue receiving standard clinical care.

- **Methodology in details:** (the description should be chronological, starting with randomization method in detail if RCT, group allocation and characteristics of each group. Also, indicate what would be done to participants initially and at follow-up visits, including the follow-up duration, if applicable.

Randomization & Allocation: Computer-generated random sequence (1:1 ratio), randomized to either cases (where IV to oral conversion will be done), or control (who will continue on IV antimicrobials). Sealed opaque envelopes will be used. The CONSORT study flow diagram will be used**.**

Data will be collected from day 1 of admission and followed up every 24 hours using a designed data collection sheet. Patient will be followed up till discharge or at least 5 days, starting from the date the patient is eligible for the conversion.

Data collection will include:
Part 1: Demographic patients' data
Part 2: Diagnosis and infectious status of the patient:

- Source of infection
- Vital signs (Heart rate, Blood pressure, Respiratory rate and temperature)
- NPO (Y /N)
- Laboratory data (CBC, CRP, liver and kidney function tests, culture results) at admission or baseline before starting the conversion, and followed up every 24 hours starting from the date the patient is eligible for the conversion.
- Antimicrobial Agents: Name, Dose, Frequency, Route, Days of therapy.

Part 3: For patients, is in the cases group: the selected oral antimicrobial`s name, Dose,

Frequency, Route, days of therapy, and its estimated cost; If not suitable for conversion, the reasons why the patient is a candidate for oral dosage form but not converted, the possible reasons, and reassess daily.

IV to PO therapy conversion strategies: based on the availability and effectiveness.

- **Sequential strategy:** replacing a parenteral version of a medication with its oral counterpart of the same compound.
- **Switch strategy:** involves the conversion of an IV medication to an oral equivalent, within the same class and with the same level of potency, but of a different compound.
- **Step-down strategy**: injectable medication is substituted with an oral agent in another class or a different medication within the same class, where the frequency, dose, and the spectrum of activity may not exactly be similar.

Oral antimicrobials used should have good bioavailability (preferably greater than 50-80%). Clinical pharmacists will play a role in the IV to PO switch criteria and personalize the most appropriate strategy for each patient, recommend the most appropriate antimicrobial, doses according to indication, age, renal function and weight. Also, spacing or holding enteral feeding from oral antimicrobials that interact with, and select the appropriate oral dosage form that doesn't clog the feeding tube.

Oral Antibiotics	Dosage form available	Dose	Current IV antibiotics	Type of conversion
Amoxicillin-Clavulanate (Hibiotic)	600 mg/5 ml suspension	90 mg amoxicillin/kg/ day in divided twice daily doses	• Ampicillin/sulbactam • Ceftriaxone	Switch and step down approach
Cefixime (Suprax)	100 mg/5 ml suspension	8 mg/kg/ day once or in divided twice daily dose	• Ampicillin/sulbactam • Ceftriaxone • Ampicillin/sulbactam+ aminoglycosides • Cefepime/Ceftazidime /Meropenem/imipenem (provided that Pseudomonas and resistant Klebsiella are excluded)	Switch and step down approach
Azithromycin	200 mg/5ml	10-12 mg/kg/dose on day 1 then 5-6 mg/kg once daily dose	Azithromycin	Sequential strategy

Metronidazole	200mg/5ml	15-50 mg/kg/day in divided three times daily	Metronidazole	Sequential strategy	

Data analysis: For converted patients (using oral dosage form) and non-converted patients (continue on intravenous form):

- Comorbid condition
- Polypharmacy
- Days of therapy (IV and PO)
- Total antibiotic acquisition costs (number of units/ day*cost*days of therapy)
- Time to suitability for conversion (days), time to actual starting PO antimicrobials
- Observation period after conversion (days)
- Length of hospital stay (days)
- Infection type (%most common type shown)
- IV antibiotics used
- Oral antibiotics used
- Complications from the IV route.
- PO to IV Percentage
- Number of patients who needed re-conversion to the IV route and causes of reswitching.
- Number of accepted/rejected recommendations for the IV to PO switch.

- **Intervention:**

- ☐ Diagnostic intervention (please describe):

  ■ Therapeutic intervention (please describe): patients will be randomized to either cases (where IV to oral conversion will be done) or the control group (who will continue on IV antimicrobials).

- ☐ intervention

- **Does the research involve?**

  ■ Human participants

  ☐ Biological samples/Tissues

  ☐ Identifiable private data/Information

- **Type of consent of study participants:**

  ■ Written consent

  ☐ No consent needed (Please justify)

- **Potential risks:**
  (Please mention all risks involved, even mild ones as pain, discomfort, chance of infection or psychological effects)

- Infection recurrence
- Treatment failure requiring IV antibiotics

Risk mitigation include:

- Strict eligibility criteria for switching
- Continuous clinical monitoring
- Immediate re-initiation of IV therapy if deterioration occurs
- Choose an antimicrobial oral dosage form with good bioavailability
- Difficult source control infections will be excluded.
- Patients with any condition that will affect oral absorption will be excluded

Moreover, the study intervention follows international antimicrobial stewardship guidelines (CDC and WHO), which support IV-to-PO conversion in clinically stable patients.

- **Confidentiality of data:** (Please explain how privacy and confidentiality of data and records will be maintained)

All information collected during this study will be kept confidential, with accessibility restricted to the authorised members of the research team only, and will be used for research purposes only. No personal identifiers (name, ID, medical record number) will be used in data collection or data analysis. Study results will be reported in aggregate form only, and no individual participant will be identifiable. After the period of the study, data will be securely destroyed according to the institutional guidelines.

9- Study outcomes:

- **Primary outcomes** (Most important measurable outcomes)

  Efficacy and safety of IV to PO antimicrobial conversion (infectious markers, and radiological evidence of infection)

- **Secondary outcome parameters** (other outcomes to be assessed)

  1- Length of hospital stay.

  2-Rate of re-admission of re-converted patients

  3- Cost differences between IV and PO dosage forms

Efficacy is defined as:

- Improvement of clinical symptoms, and infection markers (Temperature, CRP, WBCs)
- No need to re-escalate to IV antibiotics
- No new infection complications

Treatment failure is defined as:

- Persistent fever after switch, elevated CRP, WBCs
- Clinical deterioration

- Infection-related readmission within 7 days

Time-point of assessment:

- Baseline
- Day of eligibility of IV-to-PO switch
- During the 7 days after conversion
- Day 14 follow-up

Objective measures:

- Duration of IV, PO antibiotic therapy (days)
- Total antibiotic duration
- Length of hospital stay
- Treatment success rate
- Rate of antibiotic-related adverse events
- Rate of recurrence within 14 days
- Rate of reconverted patients to IV therapy

10- Sample size and technique (number of study subjects included and justification, including the clinical and statistical assumptions supporting sample size calculation)

According to Petithomme-Nanrocki et al., 2023[16], the proportion of success rate in IV and PO antibiotics were 84% and 95%, respectively. The sample size was calculated to achieve a power of 80% (at an alpha error of 0.05), using sealedenvelope.com/power/binary-noninferior sofware. The minimum required sample size is 28 cases and a similar number for control; therefore, a minimum of 64 patients will be required using 10% dropout.

11- Statistical analysis (Please describe your data analysis plan)

Statistical analysis will include:

- Descriptive statistics for baseline characteristics
- Chi-square test for categorical variables (success rate-recurrence rate-re-switch rate)

- Independent t-test for continuous variables
- Kaplan-Meier analysis for time-to-event outcomes (e.g., treatment success)

Statistical significance will be set at $p < 0.05$.

12- Source of funding: (Please include source of funding, even if self-funding)

- Faculty of Medicine, Cairo University ■
- Other sources: ☐

Please specify: There is no direct funding from any agents. However, the facilities of Cairo University Hospital will be used in this study. Because the study subjects will receive treatment at Cairo University Hospital.

13- Time plan:

- When to start (**the start date should be after getting REC approval**)?
  Immediately after getting REC approval

- When expected to finish? 6-12 months

- When to publish? after finishing the data collection and writing phases (2-3 months)

14- References:

1. Pablos A. I., Escobar I., Albiñana S., Serrano O., Ferrari J. M., de Tejada A. H. Evaluation of an antibiotic intravenous to oral sequential therapy program. Pharmacoepidemiology and Drug Safety. 2005;14(1):53–59.
2. Berman J. R., Zaran F. K., Rybak M. J. Pharmacy-based antimicrobial-monitoring service. American Journal of Health-System Pharmacy. 1992;49(7):1701–1706.
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4. Senn L., Burnand B., Francioli P., Zanetti G. Improving appropriateness of antibiotic therapy: Randomized trial of an intervention to foster reassessment of

prescription after 3 days. Journal of Antimicrobial Chemotherapy. 2004;53(6):1062–1067.

5. Ray-Barruel, G., Xu, H., Marsh, N., Cooke, M. & Rickard, C. M. Effectiveness of insertion and maintenance bundles in preventing peripheral intravenous catheter-related complications and bloodstream infection in hospital patients: a systematic review. Infect. Dis. Health. 2019; 24: 152–168.

6. Ashour RH, Abdelkader EA, Hamdy O, Elmetwally M, Laimon W, Abd-Elaziz MA. The pattern of antimicrobial prescription at a tertiary health center in Egypt: a point survey and implications. Infection and Drug Resistance. 2022 Jan 1:6365-78.

7. Ez-Elarab HS, Eltony MA, Swillam SM. Appropriateness of antibiotic use at two university hospitals in Egypt. The Egyptian Journal of Community Medicine2009. 2009 Jul;27.

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9. Shams MM, Hamdy EM, Mohamed KA, Qwaider MO, El-Agha B, Elmatary SA. The pattern of antibiotics prescription and consumption: A cross–sectional study. One Health Bulletin. 2022 Jan 1;2(1):13.

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11. Pablos AI, Escobar I, Albinana S, et al. Evaluation of an antibiotic intravenous to oral sequential therapy program. Pharmacoepidemiol Drug Saf. 2005 Jan. 14(1):53-9.

12. Martinez MJ, Freire A, Castro I, et al. Clinical and economic impact of a pharmacist-intervention to promote sequential intravenous to oral clindamycin conversion. Pharm World Sci. 2000 Apr. 22(2):53-8.

13. Li JZ, Willke RJ, Rittenhouse BE, Rybak MJ. Effect of linezolid versus vancomycin on length of hospital stay in patients with complicated skin and soft tissue infections caused by known or suspected methicillin-resistant staphylococci: results from a randomized clinical trial. Surg Infect (Larchmt). 2003 Spring.

4(1):57-70.

14. Gollin G, Abarbanell A, Moores D. Oral antibiotics in the management of perforated appendicitis in children. Am Surg. 2002 Dec. 68(12):1072-4.
15. Winston DJ, Busuttil RW. Randomized controlled trial of oral itraconazole solution versus intravenous/oral fluconazole for prevention of fungal infections in liver transplant recipients. Transplantation. 2002 Sep 15. 74(5):688-95
16. Petithomme-Nanrocki M, Vernet-Garnier V, Lebrun D, Bajolet O, Bonnet M, Hentzien M, Ohl X, Diallo S, Bani-Sadr F. Early switching from intravenous to oral antibiotic therapy in bone and joint infections associated with methicillin-susceptible Staphylococcus aureus bacteremia. Infectious Diseases Now. 2023 Sep 1;53(6):104739.

1- Please fill in all the included sections and don't delete any part of the template
2- For choice brackets, please just use the fill in function in word