



MURIA GROUP

First Training Workshop And Symposium



University of Botswana _ 27th – 29th July 2015

NOVEL APPROACHES IN DRUG UTILISATION RESEARCH

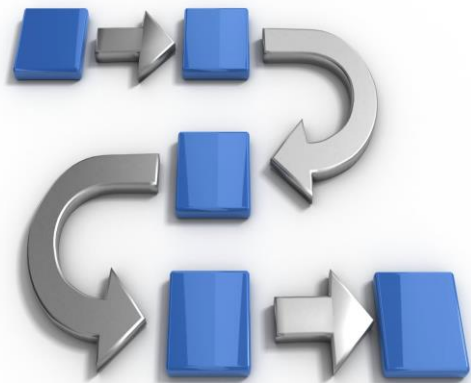
Assessing prescription appropriateness and treatment outcomes in DU studies : A novel approach in Data handling and organization for analysis.

**PRESENTER: DR MKB ADORKA, Department of
Pharmacology & Therapeutics, School of Pharmacy,
FOHS, University of Namibia**

INTRODUCTION (1)

- * **METHODOLOGY** : Definition

- * Systematic, theoretical analysis of methods applied to a field of study.



**Term used
invariably to mean
Method(s)
employed in a
study**

- * A theoretical analysis of methods and principles associated with a branch of knowledge.

INTRODUCTION (2)

- * Methodologies of drug utilisation research (DUR) greatly metamorphosed over the years since the inception of the field of study in the middle 60_s
 - * Thanks to the pioneering work of Arthur Engel of Sweden and Pieter Siderius of Holland.
- * **Developing a study method:**
 - * Study objective?
 - * What data?
 - * What analysis?
 - * What interpretation?
 - * All determinants of method to use and how to handle data

INTRODUCTION (3)

- * Data handling prior to data analysis and interpretation:
 - * Key to ease of analysis and research quality.
 - * Determined by study objective e.g.:
 - * Assessment of prescription appropriateness
 - * Assessment of effectiveness of drug treatments
 - * Involve e.g:
 - * Determining extents of prescriptions' conformities to predetermined criteria for appropriateness
 - * Comparing effectiveness of drug treatment regimens between patient groups in comparative cross-sectional studies
- * Can be mucky enough to make data analysis and interpretation a nightmare particularly in retrospective cross-sectional studies

INTRODUCTION (4)

* **Main driver of novel approaches in DUR:**

- * Responses to challenges of getting around investigating a new or rather unique research problem
- * Investigating a research problem in a way unique to one's thinking (Novel ideas)
- * Beauty of Novel approaches
 - * Makes research dynamic



INTRODUCTION (5): Examples from the literature

- * **Bain KT *et al.*:** Noticed that studies aimed at improving medication focused mainly on medication prescribing and not much emphasis on medication discontinuation.¹
 - * Proposed a formalised approach in a conceptual frame work for rationally discontinuing medications as a necessary antecedent to improving medication safety and hence the quality of care of patients
- * **Laura van Buul *et al.*:** Antimicrobial stewardship programmes (ASP) do not include in their designs physician antimicrobial prescribing behaviours despite these being necessary factors to consider.²
 - * Developed a novel approach in ASP that addressed relevant determinants of antimicrobial prescribing
 - * Participatory Action Research (PAR).

INTRODUCTION (6): Principles

* Establish need to develop a new method

- * Search literature to find out if:
 - * Your research problem has ever been investigated
 - * Research method (s) used by other investigators had any limitations ?
- * Is your novel method going to add value to or address limitations of methods used by other investigators?

* Methodological design

- * What problem?
- * Data Type:
 - * Retrospective, Prospective, Quantitative or Qualitative
- * What method of analysis?
 - * Descriptive/ inferential statistics
- * What next?
 - * Publish your methodological design as a new approach

Examples of Novel approaches in DUR: Two Lesotho studies

- * Assessing the appropriateness of antibiotic prescriptions in Lesotho public hospitals: A novel methodology based on principles of antibiotic prescribing
- * An assessment of the effects of prescribed anti-hypertensive drug therapies on blood glucose levels of maturity onset diabetic patients on treatment with oral hypoglycaemic drugs: The case of selected Health Centres in Lesotho.
 - * Poster presentation
 - * Challenges of using retrospective data in treatment effectiveness studies

A novel methodological approach in a DUR (1)

Assessing the appropriateness of antibiotic prescriptions in Lesotho public hospitals: A novel methodology based on principles of antibiotic prescribing

Adorka M, Mitonga KH, Lubbe M, Serfontein J, Allen K. ³

Focus:

A methodological presentation of handling field data in the assessment of antibiotic prescriptions for their appropriateness

Novel methodological approach in a DUR (2)

* **The Problem:**

- * Inappropriate prescribing and use of antibiotics
 - * Compromise treatment outcomes
 - * Contribute to the of antibacterial resistance development ⁴
- * Antibiotic prescribing for empiric treatment of infections:
 - * Common in medical practice
 - * Mainstay of treating infections in developing countries
 - * Lack of functional microbiology laboratories
 - * Ineffectual systems of dissemination
- * Appropriate selection of antibiotics in treating infections a major challenge in medical practice
- * Assessment of the appropriateness of antibiotic prescriptions difficult and complicated

Novel methodological approach in a DUR (3)

- * Required for health care providers to have adequate knowledge in bacteriology of infections and principles of antibiotic prescribing ^{5,6}
 - * Causative agents of infections and their antibacterial sensitivity patterns
 - * Physicochemical, pharmacokinetic and pharmacodynamic properties of antibiotics
 - * Compatibilities of antibiotics in situations of multiple antibiotic prescribing
- * Assessment of the appropriateness of antibiotic prescriptions difficult and complicated
 - * Many criteria for appropriateness need to be considered
- * **Key Questions:**
 - * How appropriate are antibiotic prescriptions?
 - * How does one go about assessing antibiotic prescriptions?

Novel methodological approach in a DUR (4)

- * Traditional prescription assessment methods involve determining extents to which antibiotics are prescribed in conformity with:
 - * Treatment guidelines
 - * Some criteria of appropriateness based on opinions of antibiotic experts.
- * **Why new approach?**
 - * A clinical environment may not have:
 - * Elaborate antibiotic treatment guidelines
 - * Available services of antibiotic experts
 - * Necessary to assess the appropriateness of antibiotic prescriptions using alternative but equally versatile procedures

Novel methodological approach in a DUR (5)

- * **Alternative procedure:**

- * Use of assessment criteria formulated from principles of antibiotic prescribing

- * **Fundamental principle:**

- * By logic prescribing antibiotics according to guiding principles would result in antibiotics being prescribed appropriately to ensure the effective treatment of infections.

Study Objective

- * To assess the appropriateness of antibiotic prescriptions using an assessment tool developed from principles of antibiotic prescribing as an alternative to traditional prescription assessment methods based on elaborate antibiotic prescribing guidelines or decisions of antibiotic experts

Methodological Design

- * Prospective cross-sectional design
- * Data description, collection & source; sample size etc
 - * Data relevant to study:
 - * Patient profile: demographic characteristics and treatment received
 - * Types of infections and procedures of infection diagnosis
 - * Prescribed antibiotics were collected from within a one month period
 - * Source and Collection:
 - * Patients' case notes (Inpatient files and Outpatient-treatment booklets)
 - * Individual data collection tools
 - * Outpatient and inpatient settings of 5 Lesotho public hospitals
 - * Sampling and sample size
 - * All antibiotic prescriptions within 1-month period of year of data collection
 - * 307 inpatient and 865 outpatient prescription records were assessed.

Methodological procedure: Data Handling & organisation (1)

* **Creation of master data file of prescription records**

- * Excel Spreadsheet
 - * Electronic field data capture
- * Data export (Statistical analysis programme)
 - * Creation of prescription assessment data
- * 2 basic parts of sheet
 1. Field data
 2. Prescription assessment data
 - Created

Methodological procedure: Data Handling & organisation (2)

* **Formulation of assessment criteria**

- * Statements on guiding principles of antibiotic prescribing developed into criteria and numbered (Tables 1 & 2)
- * Information on infections and their aetiologies and also the therapeutic and physico-chemical properties of antibiotics compiled from literature, tabulated and used as reference sources in data compilation procedures
 - * Necessary for precise decisions to be made on whether or not:
 - * Diagnoses or symptoms for which antibiotics were prescribed were of bacterial causes.
 - * A prescribed antibiotic met defined criteria on therapeutic and physiochemical properties.

Table 2: Criteria for determining appropriateness of antibiotic prescriptions for outpatients

#	Criterion definition
1	Suggestive signs and symptoms of infection present?
2	Presenting signs and symptoms absolute for bacterial infection?
3	Site of infection or possible site for infection identified?
4	Potential source of infection e.g. indwelling catheter and prosthetic devices or surgical and other open wounds present?
5	Presence of infection established by objective data?
6	Presence of infection inferred from symptoms only?
7	Antibiotic prescribed alone?
8	Prescribed dose of antibiotic correct?
9	Antibiotics in multiple therapy compatible?
10	Spectra of activity of 2 or more antibiotics in multiple antibiotic therapy similar?
11	Prescribed antibiotic (s) indicated against all possible pathogens associated with site of infection?
12	Bacterial morphological and Grams stain determined before therapy initiation?
13	Culture sensitivity test performed before initiation of or during antibiotic therapy?
14	Antibiotic choice based on culture sensitivity test results?

Table 1: Criteria for determining appropriateness of antibiotic prescriptions for inpatients

* #	Criterion definition
1	Suggestive signs and symptoms of infection present?
2	Presenting signs and symptoms absolute for bacterial infection?
3	Site of infection or possible site for infection identified?
4	Potential source of infection e.g. indwelling catheters and prosthetic devices or surgical and other open wounds present?
5	Presence of infection established by objective data?
6	Presence of infection inferred from symptoms only?
7	Antibiotic prescribed alone?
8	Initial antibiotic treatment modified by addition of other antibiotics?
9	Initial antibiotic treatment modified by substitution of other antibiotics?
10	Prescribed doses of antibiotic/antibiotics correct?
11	Antibiotics in multiple therapy compatible?
12	Spectra of activity of 2 or more antibiotics in multiple antibiotic therapy similar?
13	Prescribed antibiotic (s) indicated against all possible pathogens associated with site of infection?
14	Bacterial morphological and grams stain performed before therapy initiation?
15	Culture sensitivity test ordered before antibiotic therapy initiation?
16	Culture sensitivity test performed in the course of antibiotic therapy?
17	Antibiotic choice based on culture sensitivity test results?

Methodological procedure: Data Handling & organisation (3)

- * Criteria entered as extended variables for each record in the Excel spread sheet
- * Entries of “Yes”, “No” or “Not applicable” responses indicating prescription conformities to criteria were made
- * **Setting Conditions for Assessment**
- * Statements on criteria combinations to indicate conditions for appropriateness determination developed (Tables 3 &4)
- * Conditions numbered and also entered as extended variables on the spreadsheet
- * Statements on condition combinations developed to categorise prescriptions into predetermined categories of appropriateness (Table 5)

Table 3 Criteria combinations and their indications: OUTPATIENT DATA

Condition#	Criteria grouping	Indication
I	"Yes" for criteria 1, 2 and 3 OR "Yes" for 5	Presence of infection or need for antibiotic use for treatment established
II	"Yes" for 1, 3, and 6 and "No" for 2 and 5 OR "Yes" for 1, and 6 and "No" for 2, 3 and 5	Bacterial Infection may be present though not confirmed
III	"Yes" for criteria 3 and 4 and "No" for 1	Need for antibiotic use for prophylaxis established
IV	"No" for 1, 2, 3 and 5 Or "No" for 1, 2, and 5 and "NA" for 3	Presence of infection or need for antibiotic use for treatment NOT established
V	"No" for 1, 2, and 4 and "NA" for 3 OR "No" for 1, 2, 3 and 4	Need for prophylactic use of antibiotic NOT established
VI	"Yes for 7 and 11 OR "Yes" for 7 and 12	Principles of empiric prescribing of single antibiotic for treatment followed
VII	"No" for 7 and 10 and "Yes" for 9 and 11 OR "No" for 7 and 10 and "Yes" for 9 and 12	Principles of empiric prescribing of multiple antibiotics for treatment followed
VIII	"Yes" for 7 and "No" for 11	Principles of empiric prescribing of single antibiotic for treatment NOT followed
IX	"No" for 7 and 9 OR "No" for 7 and "Yes" for 10 OR "No" for 7 and 11	Principles of empiric prescribing of multiple antibiotics for treatment NOT followed
X	"Yes" for 13 and "No" for 14	Principles of empiric prescribing of antibiotic(s) for treatment NOT followed
XI	"No" for 8	Medication error in antibiotic prescribing
XII	"Yes" for 7, 13, and 14	Principles of antibiotic prescribing based on CST results followed
XIII	"No" for 7 and "Yes" for 9, 13, and 14	Principles of antibiotic prescribing based on CST results followed
XIV	"Yes" for 3, 4, 7, and 11	Principles of antibiotic prescribing in prophylaxis followed
XV	"Yes" for 3, 4, 9, 11 and "No" for 7 and 10	Principles of antibiotic prescribing in prophylaxis followed
XVI	"Yes" for 3, 4 and 7 and "No" for 11	Principles of antibiotic prescribing in prophylaxis NOT followed
XVII	"Yes" for 3, 4 and 10 and "No" for 7 and 9 OR "Yes" for 3, 4 and 10 and "No" for 7 and 11	Principles of antibiotic prescribing in prophylaxis NOT followed

Table 4 Criteria combinations and their indications: INPATIENT DATA

Cond #	Criteria grouping	Indication
I	"Yes" for criteria 1, 2 and 3 or 5 (i)	Presence of infection or need for antibiotic use for treatment established
II	"Yes" for criteria 1, 3 and 5(ii) and "No" for 2 and 5(i)	Bacterial Infection may be present though not confirmed
III	"Yes" for criteria 3 and 4 and "No" for criterion 1	Need for antibiotic use for prophylaxis established
IV	"No" for 1, 2, 3, and 5 (i) OR "No" for 1, 2, and 5 (i) and "NA" for 3	Presence of infection or need for antibiotic use for treatment NOT established
V	"No" for 1, 2, 3 and 4 OR "No" for 1, 2, and 4 OR "No" for 1, 2, 3 and 4 OR "No" for 1, 2, and 4 "NA" for 3	Need for antibiotic use for prophylaxis NOT established.
VI	"Yes" for 6, and 12 and "No" for 7 and 15 OR "Yes" for 6, and 13 and "No" for 7 and 15	Principles of empiric prescribing of single antibiotic for treatment followed.
VII	"No" for 6 and 11 and "No" for 7 and 15 and "Yes" for 10 and 12 OR "No" for 6 and 11 and "No" for 7 and 15 and "Yes" for 10 and 13 OR "No" for 6 and 11 and "No" for 8 and 15 and "Yes" for 10 and 12 OR "No" for 6 and 11 and "No" for 8 and 15 and "Yes" for 10 and 13	Principles of empiric prescribing of multiple antibiotics for treatment followed
VIII	"Yes" for 6 and "No" for 12	Principles of empiric prescribing of single antibiotic for treatment NOT followed
IX	"No" for 6 and 10 OR "No" for 6 and "Yes" for 11 OR "No" for 6 and 12	Principles of empiric prescribing of multiple antibiotics for treatment NOT followed
X	"Yes" for 15 and "No" for 16	Principles of empiric prescribing of antibiotic(s) for treatment NOT followed
XI	"Yes" for 7 and "No" for 14, 15 and 16 OR "Yes" for 8 and "No" for 14, 15 and 16	Principles of empiric prescribing of antibiotic(s) for treatment NOT followed
XII	"No" for 9	Medication error in antibiotic prescribing
XIII	"Yes" for 6, 15, and 16 and "No" for 7 OR "Yes" for 6, 15, and 16 and "No" for 8 OR "Yes" for 6, 15, and 16 and "Yes" for 7 OR "Yes" for 6, 15, and 16 and "Yes" for 8	Principles of antibiotic prescribing based on CST results followed
XIV	"No" for 6 and 7 and "Yes" for 10, 15, and 16 OR "No" for 6 and 8 and "Yes" for 10, 15, and 16 OR "No" for 6 and "Yes" for 7,10,15 and 16 OR "No" for 6 and "Yes" for 8,10,15 and 16	Principles of antibiotic prescribing based on CST results followed
XV	"Yes" for 3 and 4 and 6, and 12	Principles of antibiotic prescribing in prophylaxis followed
XVI	"Yes" for 3 and 4 10, 12 and "No" for 6 and 11	Principles of antibiotic prescribing in prophylaxis followed
XVII	"Yes" for 3 and 4 and 6 and "No" for 12	Principles of antibiotic prescribing in prophylaxis NOT followed
XVIII	"Yes" for 3 and 4 and "No" for 6 and 10 OR "Yes" for 3, 4 and 11 and "No" for 6 OR Yes" for 3, and 4 and "No" for 6 and 12	Principles of antibiotic prescribing in prophylaxis NOT followed

Methodological procedure: Data Handling & organisation (6)

- * **Prescription categorisation into degrees of appropriateness**
- * Conditional statements programmed into statistical software using conditional clauses to assess prescription appropriateness
- * Data imported into SAS (Statistical Analysis Software) for Windows for prescription categorisation
- * Programme ran to categorise each prescription into appropriate categories of appropriateness and entered automatically into a final new extended field for each record
- * **Master data ready for analysis according to answer research question!!!**

Table 5: Inpatient prescription appropriateness categorization

Presc. cat	Category definition	Conditions applying to prescription
A1	Antibiotic empirically prescribed in accordance with principles of antibiotic prescribing for the treatment of infection	Conditions I and VI OR Conditions I and VII apply
A2	Antibiotic empirically prescribed in accordance with principles of antibiotic prescribing for the treatment of possible infection	Conditions II and VI OR Conditions II and VII apply
B	Antibiotic empirically prescribed for the treatment of infection without adherence to the principles of antibiotic prescribing	Conditions I and VIII OR Conditions I and IX. OR Condition I and X OR Conditions I and XI apply Conditions II and VIII OR Conditions II and IX. OR Conditions II and X apply. Condition I OR Condition II OR Condition IV OR Condition VI OR Condition VII OR Condition VIII OR Condition IX OR Condition X ONLY applies
C	Antibiotic prescribed based on culture sensitivity test results	Condition XIII OR Condition XIV apply
D	Antibiotic prescribed in accordance with the principles of antibiotic prescribing for the prevention of infection	Conditions III and XV OR Conditions III and XVI apply
E	Antibiotic prescribed without adherence to the principles of antibiotic prescription for the prevention of infection	Conditions III and XVII OR Conditions III and XVIII OR Conditions III and XVIII apply Condition III OR Condition XVII OR Condition XVIII ONLY applies
F	Antibiotic empirically prescribed without adherence to principles of antibiotic prescribing and in conditions for which antibiotic prescriptions are not justified	Condition IV OR Condition V

Methodological procedure: Data Handling & organisation (7)

Excel Master Data File Projection

Study Results & Conclusions (1)

* **Results**

- * All 307 inpatient and 865 outpatient antibiotic prescriptions studied were successfully categorised into the seven predefined categories of prescription appropriateness.
- * Just about a quarter inpatient and about 3 quarters of outpatient prescriptions were appropriately prescribed for treating infections
- * About half and less than a quarter of inpatient and outpatient prescriptions comparatively inappropriately prescribed.

Study Results & Conclusions (2)

Table 7: Percentage frequency distributions of prescription categories in inpatient and outpatient departments

Antibiotic Prescription categories	Frequencies of Prescription categories			
	Inpatient Prescriptions		Outpatient Prescriptions	
	n	n%	n	n%
Prescription Category A1	55	17.9	299	34.6
Prescription Category A2	44	14.3	378	43.8
Prescription Category B	92	30	57	6.6
Prescription Category C	4	1.3	0	0
Prescription Category D	29	9.4	23	2.7
Prescription Category E	28	9.1	2	0.2
Prescription Category F	55	17.9	106	12.2
Total	307	100	865	100

Study Results & Conclusions (3)

Strength & weaknesses

* Strengths

- * Methodology employed an instrument developed from principles of antibiotic prescribing including:
 - i. Establishing presence and sites of infections prior to antibiotic prescribing; ^{6,7,8}
 - ii. Establishing potential sources of infection or comorbid conditions predisposing patients to certain infections prior to prescribing antibiotics for prophylactic reasons; ^{6,7,8}
 - iii. Establishing the need for and ensuring the effectiveness of prescribed antibiotics; ^{5,6,7,8,9,10} and
 - iv. Appropriately selecting and initiating antibiotic therapy in clinically ill or hospitalised patients. ^{7,8,11}

Study Results & Conclusions (4)

* **Weaknesses**

- * Researcher's inability to decide correctly on a prescription's conformity to criteria against which it is evaluated poses great challenge to the reliability of the methodology.
 - * Compromises results
 - * Compilation and use of data collection tools with information on infections and their causative agents and the therapeutic and physico-chemical properties of antibiotics a necessary requirement.
 - * Intensive literature review required

Study Results & Conclusions (5)

* **Conclusions**

- * Method generally assessed antibiotic prescriptions against:
 - * the establishment of the need for antibiotic use in circumstances for which the drugs were prescribed.
 - * the appropriate prescribing of the agents in respect to:
 - * therapeutic properties, efficacy, and compatibilities with co-prescribed antibiotics
 - * Generated data can be analysed in respect to a specified criterion, to provide information on sources of inappropriate prescribing.
 - * Important in the formulation antibiotic prescribing policies
- * Cheapness provided an effective means of assessing antibiotic prescriptions even in resource limited clinical environments

Study Results & Conclusions (6)

* **Conclusion**

- * Criteria formulated from principles of antibiotic prescribing had been successfully used to assess the appropriateness of antibiotic prescriptions.
- * Methodology capably classified each prescription assessed:
 - * into either of two major categories of being appropriate or inappropriate
 - * according to respective purposes and/or reasons for which antibiotics may be prescribed.
- * Has the advantage of enabling areas of antibiotic usage with associated problems to be identified and reasons for such problems to be established.

Study Results & Conclusions (7)

- * **Lesotho situation:**

- * High and low rates of inappropriate prescribing of antibiotics in the empiric treatment or prophylaxis of infections established in inpatient and outpatients settings respectively .
 - * Majority of appropriate prescriptions in out patient settings were, however, for infections with unconfirmed bacterial aetiologies.

References (1)

1. Bain KT¹, Holmes HM, Beers MH, Maio V, Handler SM, Pauker SGJ. Discontinuing medications: a novel approach for revising the prescribing stage of the medication-use process. *Am Geriatr Soc.* 2008; 56(10):1946-52.
2. LW van Buul, JJ Sikkens, MA. van Agtmael, MHH Kramer, JT van der Steen, CPMH Hertogh. Participatory action research in antimicrobial stewardship: a novel approach to improving antimicrobial prescribing in hospitals and long-term care facilities. *J Antimicrob Chemother* 2014; doi:10.1093/jac/dku068
3. Matthias Adorka, Honoré Kabwebwe Mitonga, Martie Lubbe,³ Jan Serfontein, Kirk Allen. Assessment of the appropriateness of antibiotic prescriptions in Lesotho public hospitals: a novel methodology based on principles of antibiotic prescribing. *Journal of Public Health in Africa* 2014; 5:354]
4. WHO global strategy for containment of antimicrobial resistance. http://www.who.int/drugresistance/WHO_Global_Strategy_English.pdf. (1 April 2010, date last accessed).
5. Chambers HF. Antimicrobial agents. In: Hardman, JG, Limbird LE, eds. *The pharmacological basis of therapeutics*. New York: McGraw-Hill 2001; 1143-1266.
6. Guglielmo BJ. Principles of infectious diseases. In: Koda-Kimble MA, Young LY, Alldredge BK et al. eds. *Applied therapeutics: the clinical use of drugs*. Philadelphia, Pa.: Wolters Kluwer Health/Lippincott & Wilkins, 2008; 56-1 - 56-25. 15.

References (2)

7. Finch R. Antimicrobial therapy: principles of use. *Medicine* 2005; 33: 42-46.
8. Thompson RL, Wright AJ. General principles of antimicrobial therapy. *Mayo Clin Proc* 1998; 73:995-1006.
9. Sabella C, Golfarb J. Principles of selection and use of antimicrobial agents. *Semin Pediatr Infect Dis* 1999; 10: 3-13.
10. Archer GL, Polk RE. Treatment and prophylaxis of bacterial infections. In: Kasper, DL, Brunwald E, Fauci AS, et al. eds. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill 2005; 789-806.
11. Barlett JG, Dowell SF, Mandel LA et al.. Practice guidelines for the management of community acquired pneumonia in adults: Infectious Disease Society of America. *Clin Infect Dis* 2000; 31: 347 - 82



THANK YOU