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Antimicrobial resistance and stewardship: protocol for a three-phase approach to develop educational resource for medical programme

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Note from the Editors: Instructions for reviewers of study protocols

Since launching in 2011, BMJ Open has published study protocols for planned or ongoing research studies. If data collection is complete, we will not consider the manuscript.

Publishing study protocols enables researchers and funding bodies to stay up to date in their fields by providing exposure to research activity that may not otherwise be widely publicised. This can help prevent unnecessary duplication of work and will hopefully enable collaboration. Publishing protocols in full also makes available more information than is currently required by trial registries and increases transparency, making it easier for others (editors, reviewers and readers) to see and understand any deviations from the protocol that occur during the conduct of the study.

The scientific integrity and the credibility of the study data depend substantially on the study design and methodology, which is why the study protocol requires a thorough peer-review.

BMJ Open will consider for publication protocols for any study design, including observational studies and systematic reviews.

Some things to keep in mind when reviewing the study protocol:

- Protocol papers should report planned or ongoing studies. The dates of the study should be included in the manuscript.
- Unfortunately we are unable to customize the reviewer report form for study protocols. As such, some of the items (i.e., those pertaining to results) on the form should be scores as Not Applicable (N/A).
- While some baseline data can be presented, there should be no results or conclusions present in the study protocol.
- For studies that are ongoing, it is generally the case that very few changes can be made to the methodology. As such, requests for revisions are generally clarifications for the rationale or details relating to the methods. If there is a major flaw in the study that would prevent a sound interpretation of the data, we would expect the study protocol to be rejected.

Antimicrobial resistance and stewardship: protocol for a three-phase approach to develop educational resource for medical programme

Short title: Protocol of medical programme educational resource development

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ABSTRACT

Introduction Antimicrobial Resistance (AMR) is one of the critical medical issues of the 21st century. Medical professionals are the primary prescribers of antimicrobials; their undergraduate education of Antimicrobial Stewardship (AMS) is considered one of the fundamental approaches in combating the issue of AMR. This education level provides a platform to bridge any gaps in their knowledge and competency in AMS. This study aims to develop an educational resource on microbes, hygiene and prudent antimicrobial use for the undergraduate medical programme. The guideline produced will then be assimilated into the existing curriculum which will help to improve the quality of education which in turn will improve rationale as the use of antimicrobials in the future.

Methods and Analysis A three-step approach consensus approach will be adopted for this study for the development of a validated medical curriculum guideline on AMR. A preliminary curriculum for the programme will be drafted from reviews of published literature including syllabi as well as national and international guidelines. A total of 26 potential sources were found to be relevant, and selected for this study. Subsequently, the drafted curriculum will be subjected for validation via online surveys by various infectious disease experts. Finally, a Delphi technique will be employed to obtain consensus on heterogeneous findings to the revised curriculum. The quantitative and qualitative responses will be analysed and discussed among the panel of researchers.

Ethics and Dissemination This study protocol has been approved by the Institute of Health Sciences Research Ethics Committee (IHSREC) of Universiti Brunei Darussalam (Reference: UBD/PAPRSBIHSREC/2020/124). Informed consent declaration will be collected prior to data collections as indication of agreement of participation in the study.

Keywords: antimicrobial stewardship, antimicrobial resistance, medicine, curriculum, syllabus, Delphi

BACKGROUND

Antimicrobials are considered one of the greatest medical developments in the last century, however, the abuse of these seemingly miracle drugs have led them to become ineffective in treating infections (1). Overtime, these microbes have gained immunity such as through gene mutations and exchange of resistant genes (2). Ineluctably, common infectious diseases like pneumonia, tuberculosis and gonorrhoea are becoming harder, if not impossible, to treat (3). As consequences, a higher morbidity and mortality rate as well as an increased in healthcare cost are the price to pay (4, 5). Therefore, the antimicrobial resistance (AMR) has become a global menace that "threatens the very core of modern medicine" (6).

One of the most leading cases on AMR involves multiple-drug resistant tuberculosis which has infected almost half a million people in 2016 alone (7). At current rates, AMR has contributed to at least 700 000 deaths annually, and projected to increase to 10 million lives annually by 2050 (5). Some data are available on the current status of AMR in Brunei Darussalam (8) but the nation has relatively one of the lowest antibiotics consumptions with an average of 5.9 defined daily dose (DDD) per 1000 population per day (9, 10). Paradoxically, an observational study found a marked increase in resistance of Neisseria Gonorrhoeae towards Quinolone with 93% in 2009 (11) compared to only 21% in 2001 (12).

During COVID-19 pandemic, the use of antibiotics has been surprisingly escalated despite its viral origin (13). A review of studies found that 72% of the hospitalized Covid-19 cases received antibiotics despite less than 10% experienced bacterial or fungal co-infections (14). These inappropriate prescriptions can lead to the higher risk of AMR (14). Furthermore, the extensive use of biocidal agents in non-clinical settings such as for personal disinfection may also escalate this phenomena (14). However, no conclusion was made based on previous reports on the effects of COVID-19 on AMR (15). In this current pandemic, the World Health Organization (WHO) has recommended the use of antibiotics in only severe cases where risk of getting infections and death is increased (13).

Various strategies have been employed to tackle the issue of AMR; Brunei Darussalam, in particular, has published the National Action Plan and the Good Antibiotic Prescribing Practice booklets (10). One of the main priorities realised is the education of the health professionals as well as undergraduate healthcare students including medicine, dentistry and pharmacy. The

education of Antimicrobial Stewardship (AMS) has been recognized as one of the essential elements in addressing the issue of AMR (16). A recent local study concluded that only 69% of the students have a good knowledge on antibiotics and AMR (10). Another study in the United Kingdom also stated that only one third of the undergraduate healthcare programmes includes all the recommended AMS principles (16).

OBJECTIVES

The general objective of this study is to develop an educational resource on microbes, hygiene and prudent antimicrobial use for undergraduate medical programme. Firstly, the educational resource developed as a result of this study will be assimilated into the existing curriculum in the local institution. Secondly, by reviewing various syllabi as well as national and international guidelines, we will be able to define the gaps in knowledge and improve the quality of education and the use of antimicrobials in the future.

METHODS/DESIGN

Study Overview

This study adopts a three-step approach in developing medical curriculum content guidelines on AMR by consensus as outlined by Annabelle Cumyn and Ilene Harris (17):

i. Initial delineation of curriculum content,
ii. Validation of curriculum content,
iii. Application of Delphi technique on debatable modification

Phase 1 - Initial delineation of curriculum content

We will produce a preliminary curriculum guideline on antimicrobials and AMR by reviewing and analysing literature primarily from published syllabi and guidelines by medical councils such as Australian Medical Council and Malaysian Medical Council.

Data Sources and Search Plan

We have extracted literatures through various methods (see Table 1). Relevant resources were extracted from searching across several databases including PubMed, SCOPUS, Web of Science

(WOS) and EBSCOhost. Furthermore, we have also identified medical schools in the Oceania region accredited with respective medical councils such as Australian Medical Council and Malaysian Medical Council. A thorough search has been done at each university's webpage for any published curriculum. There are 23 accredited medical schools in Australia by the Australian Medical Council as well as 13 and 34 accredited medical schools in Indonesia and Malaysia, respectively, by the Malaysian Medical Council. In addition to this, manual search was done using Google Advanced Search and cross reference search of selected articles.

Table 1. Summary of selected literatures detailing the search terms used, the search engine (PubMed, Scopus, Web of Science, EBSCOhost), the number of web results generated and the number selected from the results.

Search Term	Search Engine	Results	Selected
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	PubMed	750	3
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	PubMed	76	3
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	Scopus	670	3
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	Scopus	147	4
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	Web of Science (WOS)	142	2
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	Web of Science (WOS)	29	3

(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	EBSCOhost (Medline Complete	3675	1
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	EBSCOhost (Medline Complete)	372	1
N.B. Total selected: 20 Total duplicates: 17 (cross-checked with sources from each database and reference lists) Final total: 3			

The search strategy was formulated by researcher (L.C.M.) while the search itself was performed by lead researcher (A.M.Y.). The search was focused on undergraduate medicine programme curriculum combined with the research main theme 'antimicrobials' as to narrow down the search results. Overall, a total of 26 potential articles/resources will be included in the study (see Table 2). The articles' information also recorded the setting of the study and the year of publication.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- All literatures pertaining to antimicrobials and AMR from any country at all time.
- English language only.
- Medical education only.

Exclusion Criteria:

- Non-English and non-antimicrobials related literatures.
- Post-graduate and undergraduate curriculums other than medicine or general healthcare.

Table 2. Details of potential literatures/syllabi from various sources (**n = 26**).

A. Databases (PubMed, Scopus, WOS and EBSCOhost) after duplicates removed (**n = 3**)

Title	Setting	Year Published
An outcome-based approach for teaching prudent antimicrobial prescribing to undergraduate medical students: report of a Working Party of the British Society for Antimicrobial Chemotherapy	United Kingdom	2005
Development of consensus based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education	United Kingdom	2018
How to educate prescribers in antimicrobial stewardship practices	France	2013

B. Medical school's curriculum (**n = 2**)

Title	Setting	Year Published
Universiti Kebangsaan Malaysia	Malaysia	2018 - 2019
Universiti Malaya	Malaysia	-

C. Manual search (Google Advanced Search) (**n = 16**)

Title	Setting	Year Published
Medical Councils		
Curriculum of MBBS by Pakistan Medical & Dental Council & Higher Education Commission Islamabad	Pakistan	2011
Nigeria Undergraduate Medical and Dental Curriculum Template	Nigeria	2012
Competency Based Undergraduate Curriculum for the Indian Medical Graduate	India	2018
Core Curriculum of Bachelor of Medicine and Bachelor of Surgery by The Rwanda Medical and Dental Council	Rwanda	2019
Universities		
All India Institute of Medical Sciences India	India	2003
Sambalpur University	India	2012
University of Peradeniya	Sri Lanka	2013

Universiti of Dammam College of Medicine	Saudi Arabia	2014 - 2015
SRM University	India	2015
Universiti of Health Science Lahore	Pakistan	2015 - 2016
Dow University of Health Sciences	Pakistan	2016
Kerala University of Health Sciences	India	2016
Amna Inayat Medical College Pakistan	Pakistan	2017
NITTE (Deemed to be University)	India	2018
National Universiti of Medical Sciences Pakistan	Pakistan	2019 - 2020
Others		
Integrated Syllabus for MBBS Programme	United States	2014

D. Reference lists (**n = 5**)

Title	**Setting**	**Year Published**
Antimicrobial prescribing and stewardship competencies	United Kingdom	2013
Antimicrobial Stewardship Curriculum by Wake Forest School of Medicine	United States	-
European Antibiotic Awareness Day 2017: training the next generation of health care professionals in antibiotic stewardship	Europe	2017
Health Workers' Education and Training on Antimicrobial Resistance	United Kingdom	2019
WHO Competency Framework for Health Workers' Education and Training on Antimicrobial Resistance	Geneva	2018

Search Terms

Various search terms and combinations were proposed to broaden the search results. The words "bachelor medicine," "bachelor surgery," "medical," and "Bachelor of Medicine, Bachelor of Surgery OR mbbs"; "syllabus," "curriculum," "learning objective," and "learning aim";

"antimicrobial resistance"; "undergraduate"; and "stewardship" were used interchangeably. Furthermore, these terms were combined into two common search term for simplicity and to optimize time: (bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship, as well as, Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate (see Table 1).

Evaluation of Curriculum Content

All curriculum topics and learning points from all the selected resources will be identified using a previously validated broad-based search criterion (see Table 3) (18). Following the identification of learning points to be included in the curriculum, the variations between syllabi will be calculated using two methods; firstly, the percentage of learning points on AMR in the whole curriculum, secondly, the percentage of learning points in each determined level of achievement. A modified four-level Miller's pyramid (see Table 4**)** will be applied to rate the level of achievement of each individual learning point; level 1, demonstrates the knowledge; level 2, demonstrates the ability to understand knowledge in a clinical context; level 3, demonstrates behaviour in a controlled environment; level 4, demonstrates behaviour in a free-working environment (18).

Table 3. Curriculum search criteria and definitions (18)

Curriculum search criteria:
I. Anti* (wildcard search accepting antibiotic, antimicrobial or similar)
II. Resist* (wildcard search accepting resistant, resistance or similar)
III. Infect* (wildcard search accepting infection, infective, infected or similar)
IV. Stewardship
AMS/AMR definitions:
AMS: 'Optimizing the indication, selection, dosing, route of administration and duration of antimicrobial therapy to maximize clinical cure or prevention of infection while limiting the collateral damage of antimicrobial use, including toxicity, selection of pathogenic organisms and emergence of resistance'

AMR: ‘Resistance of an organism to an antimicrobial drug that was originally effective for the treatment of infections caused by it’

Table 4. Modified Miller's pyramid to rate level of perceived output for each learning points (18).

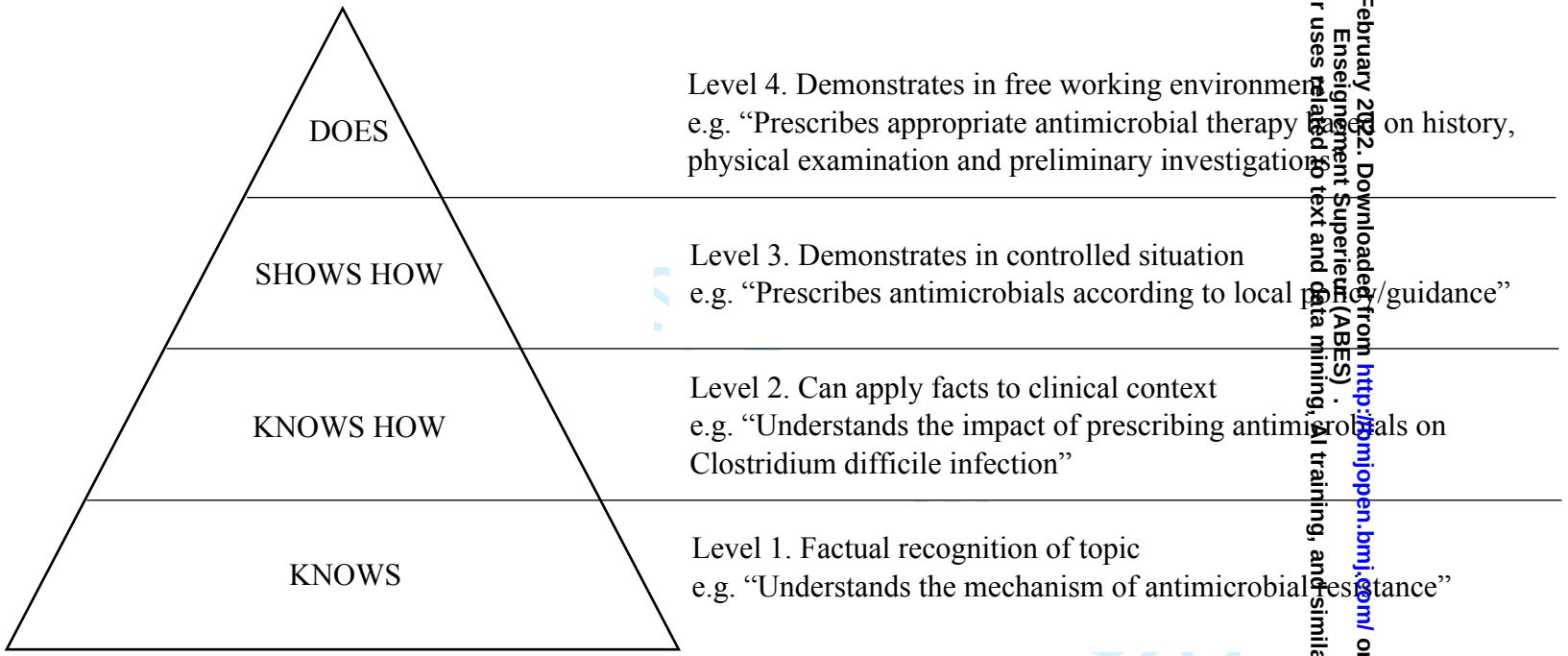
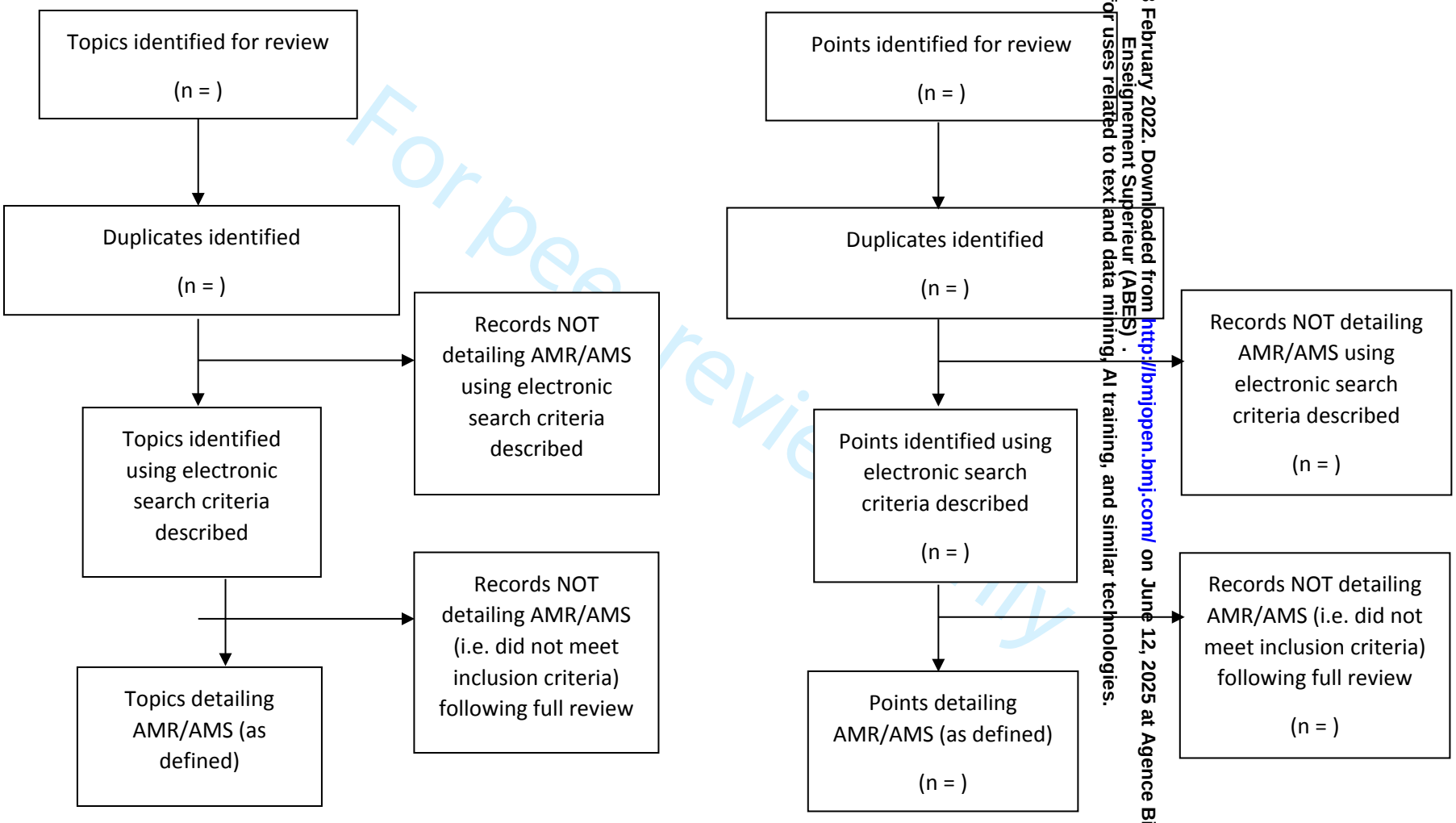


Table 5. PRISMA method to identify curriculum topics and learning points (18).

(a) Curriculum topics



Assessment of Quality of Included Studies

Contents that are essentials will be included and compiled to form a draft curriculum. Any duplications in learning points will only be counted once. The selected resources will then be assessed by the panel of researchers for the style of the drafted curriculum as well as its appropriateness, accuracy, clarity and comprehensiveness. Researchers can also suggest for any additions, modifications and deletions of contents that is suitable. Any issues arise will be discussed within the team to reach consensus. Essentially, contents that are deemed important and agreed will then be proceeded to the second phase of the research study for validation. The process of selection of curriculum topics and learning points will be based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (see Table 5) (18).

Phase 2 - Validation of the Curriculum Content

The preliminary curriculum produced from Phase 1 of this study will be validated by online quantitative and qualitative survey by a larger group of local and international experts on the field of antimicrobials and AMR.

Quantitative Survey

An online questionnaire will be made based on the curriculum composing of various topics on antimicrobials with respective learning points (see Table 6).

Table 6. Example of survey format to be used for Phase 2.

Please indicate with (✓) for each item: include / modify / delete. Suggestion(s) to include any additional items can be made in the comment section at the end of every topic.			
Topic 1: Infection Prevention and Control	**Include**	**Modify**	**Delete**
Learning Point 1: Understand the role of hand hygiene to prevent transmission of pathogens			
Justification:			
Learning Point 2: Promote principles of healthcare-associated infections (HAI) prevention and control			
Justification:			
Comment:			

Qualitative Survey

The second part of the survey includes online interviews in which experts will be for their feedback and queries on the quantitative survey. Any important modifications will be made based upon the analysis of the two surveys and will be proceeded for consensus in Phase 3.

If the outcome unanimously reached 100% rejection, the item will be removed from the curriculum. Items achieving an agreement level of 100% or less will be carried on to the phase 3.

Phase 3 - Application of Delphi technique

The modified curriculum will then be further debated via Delphi method which consists of rounds of questionnaire to obtain the experts perspectives and consensus on certain items of the topics. The results will then be collated and results will be shared within the group after each round. The experts will be allowed to modify their answers in the subsequent rounds based on the projected results. This method is chosen due to its minimal potential bias, cost and time effectiveness as well as good acceptance by majority of user.

Round 1 of Survey

In this first round, the panel of experts will be instructed to rate on a 5-point Likert scale (1 = strongly disagree; 2 = disagree; 3 = neutral; 4 = agree; 5 = strongly agree) on the level of their agreement on the proposed modifications (see Table 7). A comment space will be provided on each item for the experts to explain their perspectives.

As there is no published level of agreement, we have decided to adopt the classical criterion. Any item that achieve agreement will be accepted. Items with an agreement level between 80% to 100% will be accepted but modified according to the suggestions and advanced to the second round of survey. Items with fewer agreement will be rejected unless accompanied with comments to improve these specific items.

Table 7. Example of format to be used for Delphi survey in Phase 3.

Background Information: Here is a list of items as suggested by some respondents. We wish to remind you that the aim of the research is to develop a syllabus on antimicrobials for medicine programme; this could provide a foundation of knowledge that will enhance understanding in antimicrobial use and promote the judicious use of antimicrobials in clinical practice. For each item, please rate the extent to which you agree or disagree using the scale below.		
TOPIC 1: INFECTION PREVENTION AND CONTROL (example)		
SUGGESTED ADDITION	**RATIONALE**	**RATING** **Please use the following rating scale:** **1 = Strongly disagree** **2 = Disagree** **3 = Neutral** **4 = Agree** **5 = Strongly Agree**
To add "XXX"		Your rating: ☐ Comment:
To add "YYY"		Your rating: ☐ Comment:

Round 2 of Survey

Items that reach consensus will be included and labelled "consensus achieved" and does not requires additional debates. Items that receive necessary feedback and require further consensus will be assessed on the second round of survey. The experts will only be given the options to accept or reject the final modifications. Comment boxes will be provided only for any corrections of typographical errors. Data will be analysed similar to the round 1 of Delphi.

Post-Delphi

This stage is created to verify the final curriculum contents by the group of researchers only. Any typographical errors not identified in the previous rounds will be corrected as well as the refinement and standardization of the format will be done.

Recruitment and Identification of Experts

Experts refer to individuals who are knowledgeable and experienced on a certain subject of AMR and AMS as well as able to influence policy (19). Since there is no fixed definition of an AMR expert, we have adopted a definition which includes 'individuals reflecting expertise in prescribing and medicines management with regards to the education and practice of healthcare professionals; and antimicrobial prescribing and stewardship' (16, 20). Individuals that does not meet any of these criteria will not be included in this study.

There is also no agreement on the number of experts required for this type of study as it is dependent on the purpose and complexity of the research aim as well as the population and resources available (20). Sample size was calculated using PS Software (21). This study will require a minimum sample of 82 participants in quantitative group and 41 participants in qualitative group, with ratio of 2:1 and estimated standard deviation of 1.6 (22) with 80% certainty (power = 0.8 and alpha = 0.05). Considering different form of attritions, the minimum sample is inflated by 20%. Therefore, the expected sample size will be 100 for quantitative study group and 50 for qualitative group.

Pilot Study: A subset (5 to 10) of experts will be contacted and a pre-test will be conducted to estimate expert inputs, recruitment retention, withdrawal rates, and acceptance of evaluation measures. Participants from the pre-test will not be part of the main survey. Changes, if any, will be notified to ethics committee before proceeding with main survey.

A purposive and snowball sampling will be applied to recruit eligible experts in four countries including Australia, Brunei Darussalam, Indonesia and Malaysia. The panel of experts in this study involves qualified medical clinical academicians and medical education professionals. An initial email of invitation consisting of a participant information sheet and a consent form with the individual participant identification number (PIN) will be sent to the identified experts in these countries. Informed consent will also be obtained from participants as agreement to participate prior to commencement of data collection.

Specifically, the inclusion and exclusion criteria for participants selection are:

Inclusion Criteria:

- Qualified academicians or healthcare professionals with at least five years clinical practice experience on AMR or related disciplines
- Academic healthcare professionals involved in research and teaching of antimicrobial-related disciplines
- Prescribers and non-prescribers including medical doctors and specialists must have at least 5 years industry working experience
- Experts with academic qualifications level of a minimum basic bachelor degree

Exclusion Criteria:

- Non-experts on AMR-related field
- Other healthcare professionals not stated in inclusion criteria

Data Collection and Data Analysis

This study is expected to commence in December 2020 and to conclude in December 2021. Each round of quantitative survey will be conducted utilizing a commonly used web survey tool in the university, Qualtrics, while the qualitative surveys will be performed using Zoom software.

The participants will be sent an email containing the links to the online surveys on the specified dates. The link will be accessible for four weeks to complete and submit the questionnaire. A reminder email will be sent to any non-responders on the second week of the data collection.

Data obtained will be analysed using RStudio software for Windows. Descriptive and inferential statistics will be done to analyse quantitative survey responses. A qualitative analysis of the justifications will be performed amongst the panel of researchers.

Ethical Consideration

Ethical approval was obtained from the Institute of Health Sciences Research Ethics Committee (IHSREC) of Universiti Brunei Darussalam (UBD/PAPRSBIHSREC/2020/124).

Experts who understand the terms and conditions and agrees to participate will have to complete and sign the given consent form designated with their PIN. Identified experts will initially be explained about this research study as well their expected roles and rights to avoid conflicts during the duration of the study. Their participation will be completely voluntary and they are free to withdraw without justification by informing the researcher their PIN number. However, data from previous set of questionnaires submitted will not be removed from the analysis and publication. No personal disclosing information is to be collected to ensure anonymity. Experts will only be asked to state their age, place and years of practice, principal role as well as their qualifications. Participants will only be asked to provide their name and on the informed consent form as to be acknowledge as a member of the expert panel in publications of the study. Furthermore, all information will be kept confidential and locked in a password-protected computer and accessible to the research team only.

Patient and Public Involvement

No patient involved

DISCUSSION

The knowledge and competency of medical professionals will definitely ensure the highest quality of healthcare and this can be achieved by ensuring a robust foundation in their knowledge. Furthermore, a standardized curriculum syllabus will not only be helpful to the higher education institutions and educators, but also function as a guidance for the students learning. To the best of our knowledge, the current antimicrobial and AMR curriculum for undergraduate medical education in the region has not been validated nor there has been any study conducted to validate or develop a robust draft.

This research study will produce a locally-tailored curriculum based on reviews of curriculums and literatures and further validations by consensus among experts on antimicrobials and AMR in the region. This study will address any gaps in the curriculum particularly on antimicrobials and AMR. The curriculum produced will then be assimilated into the existing medicine programmes which overall will hopefully result in a positive solution on the escalating issue of AMR.

This study will have some limitations. The survey includes panel of experts from limited countries and may not completely represents the international medical experts. Therefore, the findings of this study might not be generalized globally. Furthermore, the curriculum that will be produced is time-limited and will require revisions over time in accordance to the development in antimicrobials and AMR.

LIST OF ABBREVIATIONS

AMR: Antimicrobial Resistance

AMS: Antimicrobial Stewardship

DDD: Defined daily dose

IHSREC: Institute of Health Sciences Research Ethics Committee

MBBS: Bachelor of Medicine, Bachelor of Surgery

PIN: participant identification number

PRISMA Preferred Reporting Items for Systematic Review and Meta-Analysis

WoS: Web of Science

DECLARATIONS

Ethics approval and consent to participate

The proposal has been fully reviewed and approved by the Institute of Health Sciences Research and Ethics Committee (IHSREC), Universiti Brunei Darussalam (UBD/PAPRSBIHSREC/2020/124). Consent will be sought from potential participant in order to participate in this study.

Consent for publication

N/A

Competing interests

The authors declare no conflicts of interest and no competing financial interest.

Authors' Contributions

L.C.M. schemed out the framework and design of the search strategy. A.M.Y wrote and developed the study protocol. A.M.Y., Z.H., M.E.A., J.S.D., S.H.M., and H.A.R. revised and reviewed the final protocol. All the authors have read and approved the final version.

Availability of data and materials

Entire data is presented in the paper, no additional data are available.

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Protocol for a three-phase prospective study to develop educational resource of antimicrobial resistance and stewardship for medical programme

Short title: Protocol of medical programme educational resource development

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ABSTRACT

Introduction Antimicrobial Resistance (AMR) is one of the critical medical issues of the 21st century. Medical professionals are the primary prescribers of antimicrobials; their undergraduate education of Antimicrobial Stewardship (AMS) is considered one of the fundamental approaches in combating the issue of AMR. This education level provides a platform to bridge any gaps in their knowledge and competency in AMS. This study aims to develop an educational resource on microbes, hygiene and prudent antimicrobial use for the undergraduate medical programme. The guideline produced will then be assimilated into the existing curriculum which will help to improve the quality of education which in turn will improve rationale as the use of antimicrobials in the future.

Methods and Analysis A three-step approach consensus approach will be adopted for this study for the development of a validated medical curriculum guideline on AMR. A preliminary curriculum for the programme will be drafted from reviews of published literature including syllabi as well as national and international guidelines. A total of 26 potential sources were found to be relevant, and selected for this study. Subsequently, the drafted curriculum will be subjected for validation via online surveys by various infectious disease experts. Finally, a Delphi technique will be employed to obtain consensus on heterogeneous findings to the revised curriculum. The quantitative and qualitative responses will be analysed and discussed among the panel of researchers.

Ethics and Dissemination This study protocol has been approved by the Institute of Health Sciences Research Ethics Committee (IHSREC) of Universiti Brunei Darussalam (Reference: UBD/PAPRSBIHSREC/2020/124). Informed consent declaration will be collected prior to data collections as indication of agreement of participation in the study. Results will be made available to medical educators and also researchers on antimicrobial resistance and stewardship. The results also will be disseminated at feedback sessions to officers at Ministry of Health and Ministry of Education, Brunei Darussalam.

Keywords: Antimicrobial stewardship, Drug Utilization Review, Drug Resistance, Microbial, Delphi Technique, Curriculum

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This protocol presents the first application of Delphi method in the antimicrobial resistance field for professional medical degree that could lead to full consensus curriculum alignment
- Triphasic validated consensus method will be used to develop a future-proof antimicrobial resistance curriculum for professional medicine programme
- To minimise this limitation, a comprehensive recruitment process involving a systematic review and snowball technique will be used, to ensure a representative range of international researchers and clinicians involved in exercise are invited to participate in the survey
- Need-based educational resource on microbes and rational antimicrobial prescribing and content priorities related to medical clinical practice are produced and validated by international panels
- The acceptance of the developed antimicrobial resistance curriculum need to be tested among wider international medical fraternity using further quantitative survey

BACKGROUND

Antimicrobials are considered one of the greatest medical developments in the last century, however, the abuse of these seemingly miracle drugs have led them to become ineffective in treating infections [1] Overtime, these microbes have gained immunity such as through gene mutations and exchange of resistant genes [2] Ineluctably, common infectious diseases like pneumonia, tuberculosis and gonorrhoea are becoming harder, if not impossible, to treat.[3] As consequences, a higher morbidity and mortality rate as well as an increased in healthcare cost are the price to pay.[4 5] Therefore, the antimicrobial resistance (AMR) has become a global menace that "threatens the very core of modern medicine". [6 7]

One of the most leading cases on AMR involves multiple-drug resistant tuberculosis which has infected almost half a million people in 2016 alone.[8] At current rates, AMR has contributed to at least 700 000 deaths annually, and projected to increase to 10 million lives annually by 2050.[5] Some data are available on the current status of AMR in Brunei Darussalam [9] but the nation has relatively one of the lowest antibiotics consumptions with an average of 5.9 defined daily dose (DDD) per 1000 population per day.[10 11] Paradoxically, an observational study found a marked

increase in resistance of *Neisseria Gonorrhoeae* towards Quinolone with 93% in 2009 [12] compared to only 21% in 2001.[13]

During COVID-19 pandemic, the use of antibiotics has been surprisingly escalated despite its viral origin.[14] A review of studies found that 72% of the hospitalized COVID-19 cases received antibiotics despite less than 10% experienced bacterial or fungal co-infections.[15] These inappropriate prescriptions can lead to the higher risk of AMR.[15] Furthermore, the extensive use of biocidal agents in non-clinical settings such as for personal disinfection may also escalate this phenomena.[15] However, no conclusion was made based on previous reports on the effects of COVID-19 on AMR.[16] In this current pandemic, the World Health Organization (WHO) has recommended the use of antibiotics in only severe cases where risk of getting infections and death is increased.[14]

Various strategies have been employed to tackle the issue of AMR; Brunei Darussalam, in particular, has published the National Action Plan and the Good Antibiotic Prescribing Practice booklets.[11 17] One of the main priorities realised is the education of the health professionals as well as undergraduate healthcare students including medicine, dentistry and pharmacy. The education of Antimicrobial Stewardship (AMS) has been recognized as one of the essential elements in addressing the issue of AMR[18] A recent local study concluded that only 69% of the students have a good knowledge on antibiotics and AMR.[11] Another study in the United Kingdom also stated that only one third of the undergraduate healthcare programmes includes all the recommended AMS principles.[19]

OBJECTIVES

The general objective of this study is to develop an educational resource on microbes, hygiene and prudent antimicrobial use for undergraduate medical programme. Firstly, the educational resource developed as a result of this study will be assimilated into the existing curriculum in the local institution. Secondly, by reviewing various syllabi as well as national and international guidelines, we will be able to define the gaps in knowledge and improve the quality of education and the use of antimicrobials in the future.

METHODS/DESIGN

Study Overview

This study adopts a three-step approach in developing medical curriculum content guidelines on AMR by consensus as outlined by Annabelle Cumyn and Ilene Harris.[20]:

i. Initial delineation of curriculum content,
ii. Validation of curriculum content,
iii. Application of Delphi technique on debatable modification

Phase 1 - Initial delineation of curriculum content

We will produce a preliminary curriculum guideline on antimicrobials and AMR by reviewing and analysing literature primarily from published syllabi and guidelines by medical councils such as Australian Medical Council and Malaysian Medical Council.

Data Sources and Search Plan

We have extracted literatures through various methods (see Table 1). Relevant resources were extracted from searching across several databases including PubMed, SCOPUS, Web of Science (WOS) and EBSCOhost. Furthermore, we have also identified medical schools in the Oceania region accredited with respective medical councils such as Australian Medical Council and Malaysian Medical Council. A thorough search has been done at each university's webpage for any published curriculum. There are 23 accredited medical schools in Australia by the Australian Medical Council as well as 13 and 34 accredited medical schools in Indonesia and Malaysia, respectively, by the Malaysian Medical Council. In addition to this, manual search was done using Google Advanced Search and cross reference search of selected articles.

Table 1. Summary of selected literatures detailing the search terms used, the search engine (PubMed, Scopus, Web of Science, EBSCOhost), the number of web results generated and the number selected from the results.

Search Term	Search Engine	Results	Selected
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	PubMed	750	3
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	PubMed	76	3

(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	Scopus	670	3
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	Scopus	147	4
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	Web of Science (WOS)	142	2
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	Web of Science (WOS)	29	3
(Bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship	EBSCOhost (Medline Complete	3675	1
Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate	EBSCOhost (Medline Complete)	372	1
N.B. Total selected: 20 Total duplicates: 17 (cross-checked with sources from each database and reference lists) Final total: 3			

The search strategy was formulated by researcher (L.C.M.) while the search itself was performed by lead researcher (A.M.Y.). The search was focused on undergraduate medicine programme curriculum combined with the research main theme 'antimicrobials' as to narrow down the search results. Overall, a total of 26 potential articles/resources will be included in the study (see Table 2). The articles' information also recorded the setting of the study and the year of publication.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- All literatures pertaining to antimicrobials and AMR from any country at all time.

- English language only.
- Medical education only.

Exclusion Criteria:

- Non-English and non-antimicrobials related literatures.
- Post-graduate and undergraduate curriculums other than medicine or general healthcare.

Table 2. Details of potential literatures/syllabi from various sources (**n = 26**).

A. Databases (PubMed, Scopus, WOS and EBSCOhost) after duplicates removed (**n = 3**)

Title	**Setting**	**Year Published**
An outcome-based approach for teaching prudent antimicrobial prescribing to undergraduate medical students: report of a Working Party of the British Society for Antimicrobial Chemotherapy	United Kingdom	2005
Development of consensus based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education	United Kingdom	2018
How to educate prescribers in antimicrobial stewardship practices	France	2013

B. Medical school's curriculum (**n = 2**)

Title	**Setting**	**Year Published**
Universiti Kebangsaan Malaysia	Malaysia	2018 - 2019
Universiti Malaya	Malaysia	-

C. Manual search (Google Advanced Search) (**n = 16**)

Title	**Setting**	**Year Published**
Medical Councils		
Curriculum of MBBS by Pakistan Medical & Dental Council & Higher Education Commission Islamabad	Pakistan	2011

Nigeria Undergraduate Medical and Dental Curriculum Template	Nigeria	2012
Competency Based Undergraduate Curriculum for the Indian Medical Graduate	India	2018
Core Curriculum of Bachelor of Medicine and Bachelor of Surgery by The Rwanda Medical and Dental Council	Rwanda	2019
Universities		
All India Institute of Medical Sciences India	India	2003
Sambalpur University	India	2012
University of Peradeniya	Sri Lanka	2013
Universiti of Dammam College of Medicine	Saudi Arabia	2014 - 2015
SRM University	India	2015
Universiti of Health Science Lahore	Pakistan	2015 - 2016
Dow University of Health Sciences	Pakistan	2016
Kerala University of Health Sciences	India	2016
Amna Inayat Medical College Pakistan	Pakistan	2017
NITTE (Deemed to be University)	India	2018
National Universiti of Medical Sciences Pakistan	Pakistan	2019 - 2020
Others		
Integrated Syllabus for MBBS Programme	United States	2014

D. Reference lists (**n = 5**)

Title	**Setting**	**Year Published**
Antimicrobial prescribing and stewardship competencies	United Kingdom	2013
Antimicrobial Stewardship Curriculum by Wake Forest School of Medicine	United States	-
European Antibiotic Awareness Day 2017: training the next generation of health care professionals in antibiotic stewardship	Europe	2017

Health Workers' Education and Training on Antimicrobial Resistance	United Kingdom	2019
WHO Competency Framework for Health Workers' Education and Training on Antimicrobial Resistance	Geneva	2018

Search Terms

Various search terms and combinations were proposed to broaden the search results. The words "bachelor medicine," "bachelor surgery," "medical," and "Bachelor of Medicine, Bachelor of Surgery OR mbbs"; "syllabus," "curriculum," "learning objective," and "learning aim"; "antimicrobial resistance"; "undergraduate"; and "stewardship" were used interchangeably. Furthermore, these terms were combined into two common search term for simplicity and to optimize time: (bachelor medicine OR bachelor surgery OR medical OR mbbs) AND (syllabus OR curriculum OR learning objective OR learning aim) AND stewardship, as well as, Antimicrobial resistance AND (syllabus OR curriculum OR learning objective OR learning aim) AND undergraduate (see Table 1).

Evaluation of Curriculum Content

All curriculum topics and learning points from all the selected resources will be identified using a previously validated broad-based search criterion (see Table 3).[21] Following the identification of learning points to be included in the curriculum, the variations between syllabi will be calculated using two methods; firstly, the percentage of learning points on AMR in the whole curriculum, secondly, the percentage of learning points in each determined level of achievement. A modified four-level Miller's pyramid (see Figure 1**)** will be applied to rate the level of achievement of each individual learning point; level 1, demonstrates the knowledge; level 2, demonstrates the ability to understand knowledge in a clinical context; level 3, demonstrates behaviour in a controlled environment; level 4, demonstrates behaviour in a free-working environment. [21]

Table 3. Curriculum search criteria and definitions [21]

Curriculum search criteria:

I. Anti* (wildcard search accepting antibiotic, antimicrobial or similar)
II. Resist* (wildcard search accepting resistant, resistance or similar)
III. Infect* (wildcard search accepting infection, infective, infected or similar)
IV. Stewardship

AMS/AMR definitions:

AMS: 'Optimizing the indication, selection, dosing, route of administration and duration of antimicrobial therapy to maximize clinical cure or prevention of infection while limiting the collateral damage of antimicrobial use, including toxicity, selection of pathogenic organisms and emergence of resistance'

AMR: 'Resistance of an organism to an antimicrobial drug that was originally effective for the treatment of infections caused by it'

Assessment of Quality of Included Studies

Contents that are essentials will be included and compiled to form a draft curriculum. Any duplications in learning points will only be counted once. The selected resources will then be assessed by the panel of researchers for the style of the drafted curriculum as well as its appropriateness, accuracy, clarity and comprehensiveness. Researchers can also suggest for any additions, modifications and deletions of contents that is suitable. Any issues arise will be discussed within the team to reach consensus. Essentially, contents that are deemed important and agreed will then be proceeded to the second phase of the research study for validation. The process of selection of curriculum topics and learning points will be based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (see Figure 2). [21]

Phase 2 - Validation of the Curriculum Content

The preliminary curriculum produced from Phase 1 of this study will be validated by online quantitative and qualitative survey by a larger group of local and international experts on the field of antimicrobials and AMR.

Quantitative Survey

An online questionnaire will be made based on the curriculum composing of various topics on antimicrobials with respective learning points (see Table 4).

Table 4. Example of survey format to be used for Phase 2.

Please indicate with (✓) for each item: include / modify / delete. Suggestion(s) to include any additional items can be made in the comment section at the end of every topic.			
Topic 1: Infection Prevention and Control	**Include**	**Modify**	**Delete**
Learning Point 1: Understand the role of hand hygiene to prevent transmission of pathogens			
Justification:			
Learning Point 2: Promote principles of healthcare-associated infections (HAI) prevention and control			

Justification:
Comment:

Qualitative Survey

The second part of the survey includes online interviews in which experts will be for their feedback and queries on the quantitative survey. Any important modifications will be made based upon the analysis of the two surveys and will be proceeded for consensus in Phase 3.

If the outcome unanimously reached 100% rejection, the item will be removed from the curriculum. Items achieving an agreement level of 100% or less will be carried on to the phase 3.

Phase 3 - Application of Delphi technique

The modified curriculum will then be further debated via Delphi method which consists of rounds of questionnaire to obtain the experts perspectives and consensus on certain items of the topics.[22] The results will then be collated and results will be shared within the group after each round.[23] The experts will be allowed to modify their answers in the subsequent rounds based on the projected results. This method is chosen due to its minimal potential bias, cost and time effectiveness as well as good acceptance by majority of user.[24 25] The planned start and end dates for the study are 1st February 2022 and 30th January 2023.

Round 1 of Survey

In this first round, the panel of experts will be instructed to rate on a 5-point Likert scale (1 = strongly disagree; 2 = disagree; 3 = neutral; 4 = agree; 5 = strongly agree) on the level of their agreement on the proposed modifications (see Table 5). A comment space will be provided on each item for the experts to explain their perspectives.

As there is no published level of agreement, we have decided to adopt the classical criterion. Any item that achieve agreement will be accepted. Items with an agreement level between 80% to 100% will be accepted but modified according to the suggestions and advanced to the second round of survey. Items with fewer agreement will be rejected unless accompanied with comments to improve these specific items.

Table 5. Example of format to be used for Delphi survey in Phase 3.

Background Information: Here is a list of items as suggested by some respondents. We wish to remind you that the aim of the research is to develop a syllabus on antimicrobials for medicine programme; this could provide a foundation of knowledge that will enhance understanding in antimicrobial use and promote the judicious use of antimicrobials in clinical practice. For each item, please rate the extent to which you agree or disagree using the scale below.		
TOPIC 1: INFECTION PREVENTION AND CONTROL (example)		
SUGGESTED ADDITION	**RATIONALE**	**RATING** **Please use the following rating scale:** **1 = Strongly disagree** **2 = Disagree** **3 = Neutral** **4 = Agree** **5 = Strongly Agree**
To add "XXX"		Your rating: ☐ Comment:
To add "YYY"		Your rating: ☐ Comment:

Round 2 of Survey

Items that reach consensus will be included and labelled "consensus achieved" and does not requires additional debates. Items that receive necessary feedback and require further consensus will be assessed on the second round of survey. The experts will only be given the options to accept or reject the final modifications. Comment boxes will be provided only for any corrections of typographical errors. Data will be analysed similar to the round 1 of Delphi.

Post-Delphi

This stage is created to verify the final curriculum contents by the group of researchers only. Any typographical errors not identified in the previous rounds will be corrected as well as the refinement and standardization of the format will be done.

Recruitment and Identification of Experts

Experts refer to individuals who are knowledgeable and experienced on a certain subject of AMR and AMS as well as able to influence policy.[26] Since there is no fixed definition of an AMR expert, we have adopted a definition which includes 'individuals reflecting expertise in prescribing and medicines management with regards to the education and practice of healthcare professionals; and antimicrobial prescribing and stewardship'.[19 27] Individuals that does not meet any of these criteria will not be included in this study.

There is also no agreement on the number of experts required for this type of study as it is dependent on the purpose and complexity of the research aim as well as the population and resources available.[27] Sample size was calculated using PS Software.[28] This study will require a minimum sample of 82 participants in quantitative group and 41 participants in qualitative group, with ratio of 2:1 and estimated standard deviation of 1.6 (22) with 80% certainty (power = 0.8 and alpha = 0.05). Considering different form of attritions, the minimum sample is inflated by 20%. Therefore, the expected sample size will be 100 for quantitative study group and 50 for qualitative group.

Pilot Study: A subset (5 to 10) of experts will be contacted and a pre-test will be conducted to estimate expert inputs, recruitment retention, withdrawal rates, and acceptance of evaluation measures. Participants from the pre-test will not be part of the main survey. Changes, if any, will be notified to ethics committee before proceeding with main survey.

A purposive and snowball sampling will be applied to recruit eligible experts in four countries including Australia, Brunei Darussalam, Indonesia and Malaysia. The panel of experts in this study involves qualified medical clinical academicians and medical education professionals. An initial email of invitation consisting of a participant information sheet and a consent form with the individual participant identification number (PIN) will be sent to the identified experts in these countries. Informed consent will also be obtained from participants as agreement to participate prior to commencement of data collection.

Specifically, the inclusion and exclusion criteria for participants' selection are:

Inclusion Criteria:

- Qualified academicians or healthcare professionals with at least five years clinical practice experience on AMR or related disciplines
- Academic healthcare professionals involved in research and teaching of antimicrobial-related disciplines
- Prescribers and non-prescribers including medical doctors and specialists must have at least 5 years industry working experience
- Experts with academic qualifications level of a minimum basic bachelor degree

Exclusion Criteria:

- Non-experts on AMR-related field
- Other healthcare professionals not stated in inclusion criteria

Data Collection and Data Analysis

Each round of quantitative survey will be conducted utilizing a commonly used web survey tool in the university, Qualtrics, while the qualitative surveys will be performed using Zoom software.

The participants will be sent an email containing the links to the online surveys on the specified dates. The link will be accessible for four weeks to complete and submit the questionnaire. A reminder email will be sent to any non-responders on the second week of the data collection.

Data obtained will be analysed using RStudio software for Windows. Descriptive and inferential statistics will be done to analyse quantitative survey responses. A qualitative analysis of the justifications will be performed amongst the panel of researchers.

Ethics and dissemination

Ethical approval was obtained from the Institute of Health Sciences Research Ethics Committee (IHSREC) of Universiti Brunei Darussalam (UBD/PAPRSBIHSREC/2020/124).

Experts who understand the terms and conditions and agrees to participate will have to complete and sign the given consent form designated with their PIN. Identified experts will initially be explained about this research study as well their expected roles and rights to avoid conflicts during the duration of the study. Their participation will be completely voluntary and they are free to withdraw without justification by informing the researcher their PIN number. However, data from previous set of questionnaires submitted will not be removed from the analysis and publication. No personal disclosing information is to be collected to ensure anonymity. Experts will only be asked to state their age, place and years of practice, principal role as well as their qualifications. Participants will only be asked to provide their name and on the informed consent form as to be acknowledge as a member of the expert panel in publications of the study. Furthermore, all information will be kept confidential and locked in a password-protected computer and accessible to the research team only.

Results will be made available to medical educators and also researchers on antimicrobial resistance and stewardship. The results also will be disseminated at feedback sessions to officers at Ministry of Health and Ministry of Education, Brunei Darussalam.

Patient and Public Involvement

No patient or public is involved in this study.

DISCUSSION

The knowledge and competency of medical professionals will definitely ensure the highest quality of healthcare and this can be achieved by ensuring a robust foundation in their knowledge. Furthermore, a standardized curriculum syllabus will not only be helpful to the higher education institutions and educators, but also function as a guidance for the students learning. To the best of our knowledge, the current antimicrobial and AMR curriculum for undergraduate medical education in the region has not been validated nor there has been any study conducted to validate or develop a robust draft.

This research study will produce a locally-tailored curriculum based on reviews of curriculums and literatures and further validations by consensus among experts on antimicrobials and AMR in the region. This study will address any gaps in the curriculum particularly on antimicrobials and AMR. The curriculum produced will then be assimilated into the existing medicine programmes which overall will hopefully result in a positive solution on the escalating issue of AMR.

This study will have some limitations. The survey includes panel of experts from limited countries and may not completely represents the international medical experts. Therefore, the findings of this study might not be generalized globally. Furthermore, the curriculum that will be produced is time-limited and will require revisions over time in accordance to the development in antimicrobials and AMR.

LIST OF ABBREVIATIONS

AMR: Antimicrobial Resistance

AMS: Antimicrobial Stewardship

DDD: Defined daily dose

IHSREC: Institute of Health Sciences Research Ethics Committee

MBBS: Bachelor of Medicine, Bachelor of Surgery

PIN: participant identification number

PRISMA Preferred Reporting Items for Systematic Review and Meta-Analysis

WoS: Web of Science

DECLARATIONS

Ethics approval and consent to participate

The proposal has been fully reviewed and approved by the Institute of Health Sciences Research and Ethics Committee (IHSREC), Universiti Brunei Darussalam

(UBD/PAPRSBIHSREC/2020/124). Consent will be sought from potential participant in order to participate in this study.

Consent for publication

N/A

Competing interests

The authors declare no conflicts of interest and no competing financial interest.

Authors' Contributions

L.C.M. schemed out the framework and design of the search strategy. A.M.Y wrote and developed the study protocol. J.S.D., L.C.M., S.H.M., M.E.A., J.S.D., Y.Y.K., H.R., S.K.S.D., and Z.H. revised and reviewed the final protocol. All the authors have read and approved the final version.

Availability of data and materials

Entire data is presented in the paper, no additional data are available.

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Figure legends

Figure 1. Modified Miller's pyramid to rate level of perceived output for each learning points (Modified from Reference 21).

Figure 2. PRISMA Flow Diagram

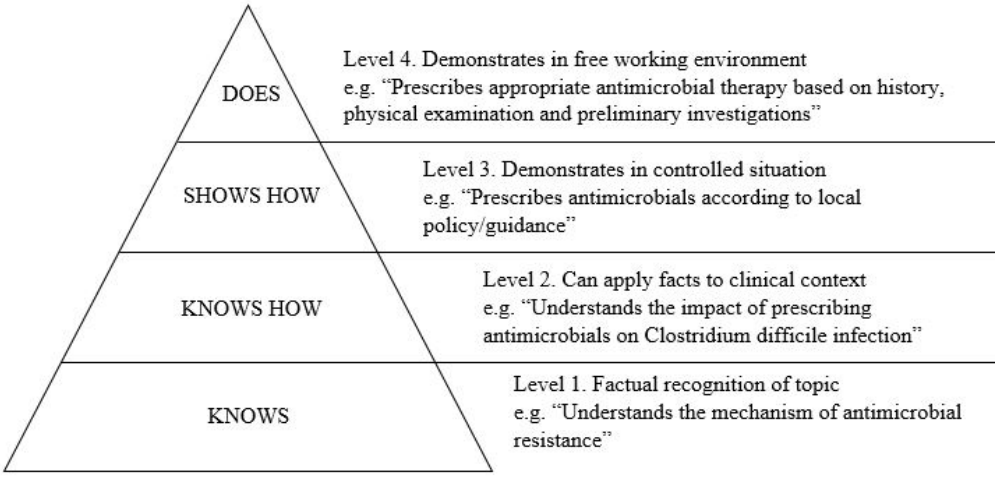
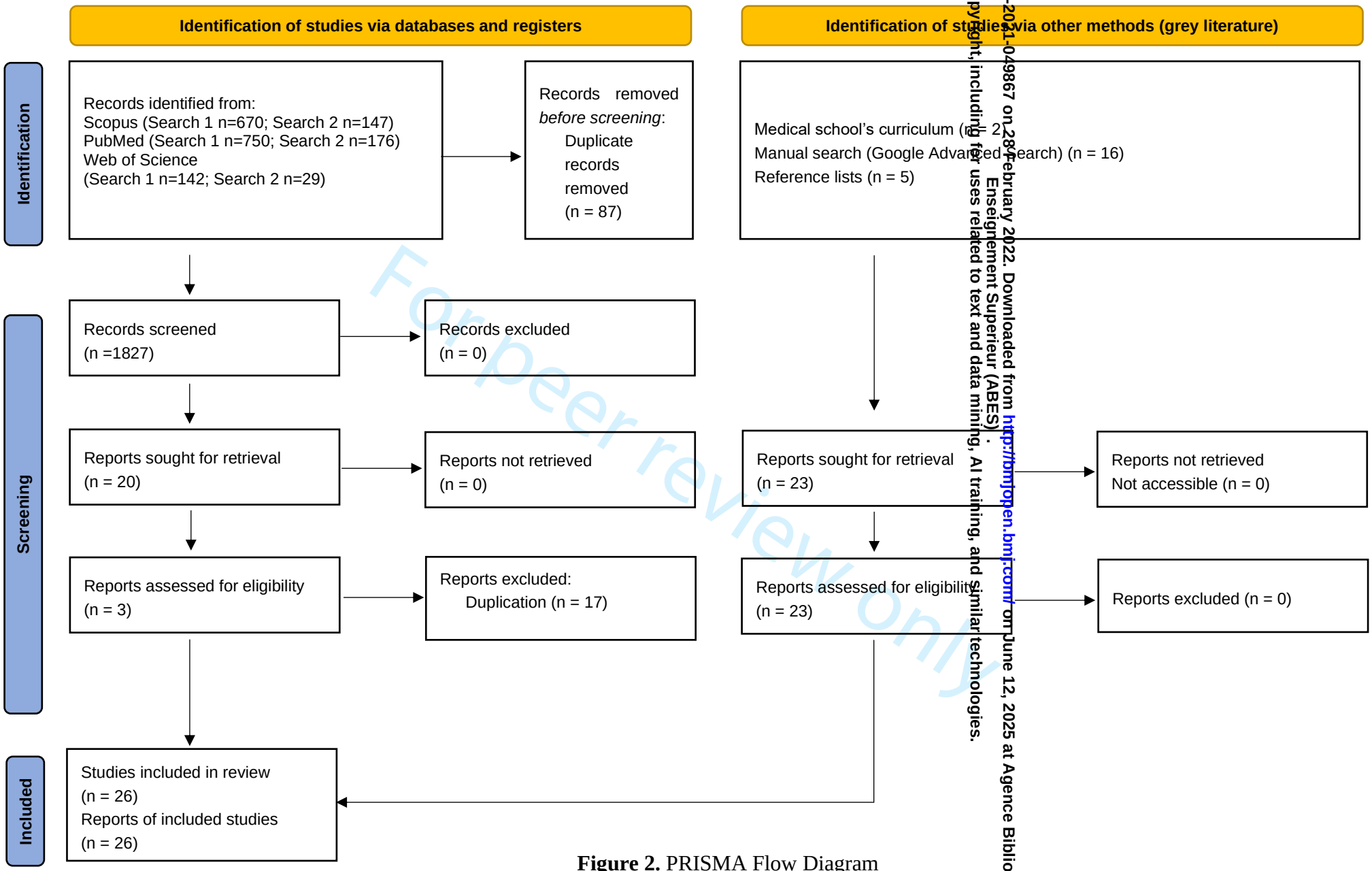


Figure 1. Modified Miller's pyramid

189x93mm (96 x 96 DPI)



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