# MEDICAL RESEARCH

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WEEK 12

RECAP FROM THE DOCTOR TO THE PREVIOUS WEEKS THAT ILLUSTRATED QUANTITATIVE RESEARCH: we covered this module with different study designs, we started with them, classifying the studies into controlled and noncontrolled assignments and we divided the uncontrolled assignments into descriptive observational studies such as case report, case series, ecological studies surveys, and cross-sectional studies and we also had the descriptive analytical studies that are the case-control and cohort studies and we mentioned that in these studies we are just observing what happening it's different from the control assignment in which the investigator will do something either they give the new treatment change, the dose, and early versus late referral for physiotherapy, the patient will be seen by Family Physician or cardiologist for hypertension management or the patient will have open surgery versus endoscopic surgery all these things are controlled assignment because we are doing something as investigative and then we discussed these study designs the advantages ,disadvantages and the key aspects of the design we also invested in training you guys how to develop your questionnaire and we said the questionnaire should depend on two things previous literature review and also the expert opinion ,when we write any questionnaire we need to start with brainstorming and writing the items that should be in the questionnaire then we wrote the questions and shared with you, problems mistakes and questionnaire design, then after that we discussed the methodology of the Proposal starting with the introduction , then we have the study design type ,study are conducted then we have the primary ,secondary outcomes and we have the inclusion-exclusion criteria , study outcomes in detail through the questionnaire of tools they are using are what the component if they're using Ready questionnaire you need to mention that it's valid for use, and to mention their ability and then we'll have the sampling technique how you're going to collect your sample and also we had a lecture on the Sampling technique we need to avoid convenience or quota sampling ,we need to follow probability sampling and most studies will require multi-stage sampling technique and then we take a summary about sample size calculation and then you need to add your references about the introduction we said that we need to have three parts of Direction the first paragraph if it's a common health problem you need to mention about the magnitude of that problem ,the prevalence of that problem, the complication rate, if it's a rare uncommon condition we'll start with the definition of that condition you need to write your objectives and based on the objectives we'll have the introduction, then the first two to three paragraphs will cover the object of the study ,what has been done, and why it's important ,the last paragraph of the introduction should cover a summary about the current situation due to limitations and there is limitation of the evidence about this use of this treatment, for the treatment of this condition we need to do this phase three controlled randomized clinical trial

- there is no national study in Jordan or sampling shown the prevalence of hypertension we need to do this cross-sectional study so you need to have justification, why you are doing the study then we'll have one- two lines about the study that you are trying to do and the main goal or the aim of the study then we write down aims and objectives and when you write the manuscript to don't write aims and objectives separately , usually we add them at the last paragraph of the introduction

- A key thing that has been seen missing from most frame programs educational programs about research across the region is the critical appraisal you need to follow initially these steps that we are going to share with you today when you write any proposal when you publish your manuscript first of all you need to do a critical appraisal of your work to improve it then when you have a reference for a journal you want to show to see the work for colleagues give them feedback you need to follow these steps for this year the coming two years ,please try to follow these steps then with time you know how to do them and the critical appraisal of any manuscript or the view of the proposal manuscript will not take you that time but please initially try to follow this checklist and they will help you actually to have good critical appraisal skills ,if you have good critical appraisal skills you'll be able to write a good proposal and a good manuscript but let's start with the survey design we'll start key question: did the study address a clear Focus question or issue? Yes, cant tell , no

-do we have the last paragraph of the study shown ,what is the main objective and you can see that in the introduction this topic is well covered for example we have the example I have given you now about the prevalence of hypertension in Jordan you'll talk initially about the hypertension prevalence in the world, in the region, complications of hypertension, risk factors, and then you'll write that to justify why you are going to do this study focused question what do you mean by focused question? I want to assess the prevalence of hypertension this is not a focused question I need to look at the prevalence of hypertension during pregnancy the prevalence of hypertension, for adult population age 18 to 69 for people above the age of 18 I need to stratify the age group then is it a national study or at certain site or City so the question should assess or measure the prevalence of hypertention among people above the age 18 at represented size in Jordan .This means this is a national study so we need to be specific about each aspect related to the study :is the search method design appropriate for answering the research question the doc has seen some proposals that need to look at the risk factors of hypertension this is and they are saying that cross-section study this is not right if you want to look at the prevalence of risk factors then you'll do cross-sectional study if you want to identify risk factor to study whether this is the risk factor or not we need to do an analytical study

-hypertension is a common disease so we need to follow cross-sectional study,so if you want to look at the distribution of risk factors prevalence these risk factors this is a cross-section study if you want to see whether this is a risk factor or not this is a cohort study

-the third point is the method of selection of subjects employees teams patients divisions described we must avoid convenient sampling you will not publish it at good Journal you are wasting your time your data is not represented want to look at the complications like type two diabetes we go to the cardiologic clinic and the hospital and you'll see for example the complication rate is 70% and this is the invalid result , these results wont be accepted because hypertensive patients will be seen at primary healthcare ,secondary and also tertiary, the most complicated difficult cases will be seen at JUH so the the data here is not representing patients in Jordan so you can't publish that 70% of hypertensive patients in Jordan have complication you just followed a convenient sample of going to the Cardiology clinic at the JUH,

-so when we evaluate the sampling technique is it selection bias ?yes or no

you have for example case-control study how the controls were selected what is a subject sample about population which is representative or not so we have it's close to point three that we need to ensure that how we stratify the sample represented sample size we need to calculate the sample size, the ideal situation I need to have the whole population but when you have a large population you want to look at the prevalence of HTN among adults in Jordan there are five- six millions and you can't go to all of them so you need to have a presentative sample,we need to calculate sample size based on that was a sample response rate achieved , I'm reaching for example , 10,000 inviting 10,000 subjects to the study only 1,000 of them accept to participate this is not acceptable response rate you need to see why people are not willing to take part in your study you have a clinical trial and you want to test different medications of hypertension, for example, you need to show that eligible subjects are willing to accept the study if they don't you need to find out why they don't accept ,sometimes we sort this issue actually during the pilot phase

- in the case of mission Miss question is likely to be valid or reliable in assessing the quality of life of patients by using for example one of the sf36 this is valid for use

-a study on Diabetes and hyperthyroidism, was a good question for assessment this is not necessary that is this tool or questionnaire or symptom checklist or Pain Scale or Etc is valid for hypertension we need to assess the literature to find that this questionnaire or tool is valid for use for hypertensive patients and also for adult hypertensive patients might be valid for your sample not for the general population sometimes we have self completed tools or questionnaires and we are Distributing the questionnaires in our language and also we need to justify that these tools are valid for use in the Arabic language as well so we need to look at the questionnaire is valid for use for disease itself and also for the language we are using with it it's face to face interview you are asking the questions and you have kept the question in English that's question in English that's okay the last thing that we need to check for the measurements or questionnaires that they are valid and reliable for the study design you are using some tools that are good for cross-section studies for surveys to show the Quality of Life, Psychology, pain, but they're not good for assessment of changes over time so we can't use them in clinical trials

- so we need to check three things when you conduct critical appraisal when you write your proposal: I'm using this questionnaire validated,I'm studying for the population for the language( I'm using it with is it English or self-completed in Arabic), and also this tool is valid for use for surveys cohort study for example or a clinical trial because some questionnaires are good in providing you with good details but they are not good in their insensitivity to changes, they will not assist with the changes or be responsive with treat what skill significance assess, we need to look at and this is in the skill plan and also in the results confidence interval is very important actually

-For example on relative risk for risk factors: avoiding dietary fibers is a risk factor for hypertension,if the relative risk is three and you have two cases, you will be asked which one is stronger risk factor when you have the first point about the competent severe, for

example, we have relative risk of three but you look at the interval it's 3 till five relative risk ODDS ratio the reference point is one unlike the T-Test that reference point is zero so if the CI (confidence interval)pass through one this is insignificant so it is an insignificant risk factor for hypertension- it is Factor but for example, this is just for the scale analysis plan as an example

-if CI is 0.3 to 5, will pass through 1 this is not significant

-0. 2 to 0.9 this is below one it did not pass through one so this is a significant factor

- ex:preventive factor aspirin will reduce the incidence for f ischemic heart disease the 0. 3 to 0.6 for example and this is significant the reference point is one it should not pass through one

- another example you have the relative risk of five you have two cases and this is significant the reference point is one it should not pass through one another example you have the relative risk of five you have two cases, one case the CI four to six, the other one is 2 to 20 the narrower confidence interval like 3 to five the more confident you are in the results and the stronger is Factor there are less variations in the outcomes

- the last point about the confidence interval we have said that the one is the reference so the more you are higher than one the stronger is this Factor if you have a relative risk of 20 is stronger than 15 than 10 so the more,you go away from the one you will have stronger respect can the results be applied to your organization to your patients if you have this is a key question you need to ask for example you find the study was done at small City or small town at once hospital and you have seen that this doesn't represent the patients in that country or that region you'll say that it's not representative,but if the sample is representative you can say that I can apply these results for my patients or my country

the second example is cross-sectional

-it is used to assess the prevalence usually there are other point prevalence at 1.5 prevalence

-that's specific type of surveys and there are cross-sectional ones did the study address a clearly and focused issue that we said that we need to satisfy the age range and the group and location in our study are assessing the prevalence of hypertension for other population in Jordan ,did the authors use an appropriate method to answer questions cross-sectional study or analytical study, clinical trial based on the question where the subjects most of these points are close to the survey subject recruit acceptable way( the response rate is acceptable and are following certain including- excluding criteria and sometimes they have excluding criteria)

- the doc reviewed recently one of the proposals where someone excluded people working at certain healthcare professionals who have diplomas they were excluded from study and he objected to that point ,there is no justification to conduct for example a study to exclude People based on their education because they are working at that site you need to include everyone who fulfil these jobs , for the inclusion criteria or exclusion criteria we can't

exclude for example someone who can't read and write someone who's for example blind subject someone we can't exclude children from our research because there are available subjects we need to consider consulting their parents but we should also conduct studies on children , pregnant women, and people with disabilities ,we need people without education ,we need to include all these groups in our research

- what are the measures?I'm accurately measuring the introduced bias for example in case control studies we said that sometimes we have interview bias we need to Blind the study participants we need to consider these points that we are following in the critical appraisal where the data collected in a way that addresses the research issue, , is it face to face interview?is it chart review from patient files? and is it complete questionnaire? then we need to justify that and we mention that sometimes the unit pilot phase we decide on the way but we need to justify what we are doing we need also to try to have face to face , self completed questioner for example you need to have a manual or , tips to describe the questions for example you have when we ask about physical activity do you exercise all the time or do you feel happy all the time or do you eat healthy life, diet all the time most of the time, little of the time ,none of the time we need to just explain these points what do you mean by all the time or most of the time most of the time for me can be most different from most of the time for you or little of the time is it little of the time during the day or little of the time during the week we need to justify all these points in the questionnaire so we need to see in The Proposal in the methodology and instructions for the self-complete questionnaire were included in the questionnaire to help participant to complete the questionnaire if you have face-to-face interview you have not read you need to write down that research coordinators received training about the data collection and they have a manual for the data collection we have studied at different sites we need to ensure that coordinators at all Sites are following certain steps or they have certain instructions about the questionnaire, we need to show that you have reached enough sample, size how the results are presented and what are the main results you are studying regarding the prevalence of disease risk factors

- first we mentioned that initially, we'll start describing the study participants other one paragraph or in the first table then we have the second paragraph the first paragraph also the results should describe who participated in the study their number their mean age their characteristics and then we'll present the main results and we have to prevent variable conditions between males and females we need to show the result for all participants differences that is rigorous

- people are looking at risk factors or complications risk factor for illnesses to see a distribution or predictors of qualitative life scores they'll do chi Square which is subjective to compounding factors the right way to look at predictors of responsive treatment predictors of complications we need to show regression analysis not chi Square

-chi square will give you an idea that there could be a correlation there but the test will give you a conclusion that this is a factor or this is a predictor for these outcomes is the regression analysis

-we need to see a discussion we need to start with the key outcome and compare it with current studies, previous studies from your country from your patient population previous studies and current studies our recent studies from the region worldwide and to justify differences if you find them between these states then that be applied is it represented results and can we generalize them or not when you write the discussion recommendations we need to write, and recommendations there that how valuable is the research this study showed important outcomes out for example complication hypertension in Jordan therefore we recommend future searches to look at interventions to reduce the incidence of complications in hypertensive patient or diabetic patients in Jordan cross-sectional studies we are looking mainly at the prevalence we prefer to do them as National studies, if you want to do as certain cities we need also to ensure that the data are just considering the presence of that specific area or city and we need to ensure that is a representative study ,so you have the last example about cross-section studies to assess the prevalence of hypertension or diabetes or rheumatoid arthritis or osteoarthritis

-if you go to our patient clinic's inpatient you are just having patients who are seeking treatment you're not assessing the prevalence in the general population this is the wrong study also if you go to the community and have studied for example from represent science in but you are only asking the subject if you have HTN or not you are just underestimating the prevalence because here we have only the known cases but if you measure the blood pressure of these subjects you'll find a good proportion of subjects with undiagnosed hypertension they have the disease but they don't know that they have

## the disease preference will be the number of known cases plus the new cases over the total population

many studies across the region that assist the self-reported prevalence of hypertension this is leading to underestimation of the true prevalance of that condition ,here in the population for example diabetes and subclinical hyperthyroidism we did differentiate National studies across the region and we found that the proportion there's a high prevalence of undiagnosed cases particularly in developing countries because we don't have a regular system for primary healthcare or family medicine or subjects can be seen regularly by the healthcare professional to assess these things

the third part of this lecture will be critical appraisal of cohort

we have 3 key things are the results valid, what are the results, and will the results be helpful locally or worldwide

--first the same thing the study addressed clearly focused issue

we use cohort study to assist and whether or not smoking is a risk factor for type two diabetes among the adult population in Jordan so we have a population we have smoking and we have type two diabetes

- how we include the subjects smokers and non-smokers, was the cohort representative defined population we defined, we have type two diabetes are we confident that at Baseline we'll ask subjects , did the authors ask the subjects whether they have diabetes or impaired

glucose function or not whether they screen them or not because we have just said that you have patient with the disease without knowing so we need to ensure that we recruited eligible subjects and we ensured at Baseline they don't have the disease so you have Baseline expectation for currently measured to minimize bias.

how we assess smoking rates for cigarettes water pipe and we quantify that for example, we have , smokers and nonsmokers I will not include ex-smokers in my study as nonsmokers because they are still at high risk of diabetes, ischemic heart disease, Etc.

what the outcome accurately measured ,how we assess the diabetes for example what is the case definition what are the investigations done during the follow up so we need to see these things and we need to ensure as we mentioned at baseline they don't have type two diabetes or prediabetes this is the key thing in cohort studies and also in case-control Studies have the authors found all important confounding factors you have smoking versus diabetes did we look at a family history of diabetes we have BMI physical activity and dietary factors all the other risk factors should be identified because smokers might have a higher incidence compared to non -smokers but if you conduct further analysis you'll find that smokers maybe they had unhealthy diet maybe a good proportion of them they had family history maybe they have obesity for example or you need to assess all these factors together we call them confounding factors because these factors will affect the outcomes of your study we conduct ,sometimes we call adjusted relative risk because we need to adjust for these compounding factors in the final lists,what the full of subjects complete enough the study is for 10 years prospective or 10 years retrospective,we need to ensure that we have complete follow up

-subjects long enough I'm having prospective study on subjects age 18 for type two diabetes if I conduct the follow up for 10 years this is insufficient time for them to Develop type two diabetes so we need to ensure that we have enough duration of follow up this is we need to assist that in the methodology of Cohort study when we read any proposal or manuscript about cohort study we need to look at the duration follow up authors must justify the duration of it: the incidence influenza among highest groups needs six months of follow up that's it but when you're looking at the incidence of cancer for someone who's taken for example aspirin at the age of 30 you need to have a follow up for 30 years

-what are the main results what is relative risk sometimes we look at absolute risk reduction based on the outcome of the study but the key thing is relative risk in cohort study, how precise the CI, is it wide or is it narrow one significant or insignificant when you write the discussion of analytical studies, case-control ,cohort studies we need always to refer to the Bradford Health criteria smoking type two diabetes we need to justify things related to the pathway of type two diabetes and correlation with smoking those graduate, those respond and did we notice differences in the incidence between light smokers and heavy smokers by number of cigarettes by duration smoking we need to consider all these factors

can be applied to the local population, for all populations worldwide do the result fit with the available evidence we need to justify that discussion this is consistent with previous studies if they don't fit with them we need to justify it is a limitation of our study or previous

studies and this is what I need to see in any publication what are the implication of this study for practice, we are not just wasting our time and resources for something that we do not utilize in our day-to-day practice or and making guidelines or recommendations ,so we need to see sufficient data, one observation study provides sufficient robust evidence but if we have a large study we can utilize that if you have a large control clinical trial we can justify that so we can make a recommendation based on this point okay and studies will provide you with risk factors for example for illnesses we can proceed after we have confirmed that this risk factor is confirmed for certain illnesses, we can take the next step will be intervention programs through clinical trials to control these risk factors

-the second part of analytical studies there are case-control studies,

the key thing in case control is the case definition and controls identification and assessment of the confounding factors but we need to follow the same questions did the study address Focus issue? do the authors use appropriate methods or answer question ?

-if not feasible to conduct Cohort study and we have selected case control study and we need to justify where following case-control studies how we recruited these subjects do we have enough number of cases of controls how we calculate the power we need to mention all these points in the methodology how we selected the controls they should be matched controls is it based on geography, based on certain things we said that controls in the case-control study should be coming from the same environment if you Have hospital patients control should be from the hospital with, they should have , match for different Factors except of having the disease itself if you have from outpatients from primary Healthcare centers we should have the controls from primary healthcare centers you have cases from the Community we have controls from the community and we need to ensure that we have enough number of controls how we have we looked at the bias, have we looked at the different confounding factors, was the investigator blinded as interviewer bias how we managed to reduce the recall bias, whether medical Notes were complete -incomplete how we handle all these factors together have you looked at the genetics socio-economic environmental medical clinical confounding factors usually stratify samples we also adjust for the confounding facts, regression Analysis, same as for the relative risk what are the results key outcome of case control studies is the Odds ratio, P value we need to look at the , , ratio size, P value we said that similar to relative risk we need to be away from one to be more significant the higher the more significant do you believe in the results have we adjusted in risk factors and also we'll try to follow Bradford Health criteria for the risk factors time sequence those the graduate strength bias possibility we need to justify our results can write our results yes or no based on the methodology and the representation of the sample and also for the adjustment for the confounding factors ,do the results fit with the available evidence yes or no? and we show data and also if the results are different we need to justify why we have different results, if you believe in your study you need to justify why people should follow your results not previous studies

-to remind you about case-control studies a key thing is case definition is the very important point then we have to ensure that we have match controls in how we select the controls and the sample size for the controls and cases and then we have the odds ratio calculation

last section of this presentation is the checklist for randomized control trials

the doc is not expecting a medical student to conduct clinical trials during the academic years but I'm expecting students to be able to understand published clinical trials and to conduct critical appraisal, you'll have the fourth fifth final year you will conduct for example some presentations some important studies we'll just have summarized this clinical trial and present it to your colleagues, it's very important that you follow this checklist of clinical trials to see whether you are going to accept the results or not we'll see many hundreds of clinical trials are published on monthly basis sometimes on weekly basis we need to take the valid ones the ones with critical appraisal and can accept the result of these studies you'll see many clinical trials will not accept the result because of bias or limitations of these studies I need to emphasize **critical appraisal doesn't mean looking for limitations critical appraisal is evaluating the study we need to mention the strength points that the authors have clear case definition the authors have enough sample size tools of assessment that are valid and reliable it's not just looking for the limitations, critical appraisal means that looking at as constructive appraisal looks at the strength and limitations of these manuscripts or proposals what the objective of the trial sufficiently** described and have a new treatment to compare the new treatment and existing treatment to compare late referral to compare different doses of treatment satisfactory statement, given the diagnostic criteria who should be included in the trial any patient with type two diabetes or patient with HBA1C above 10 or patient with HBA1C of 6.5 to 10 we need to justify to mention who should be included in the trial where the controls and who's the cases who is the control are all subjects in the study are at equal chance to be included in the treatment or the control arm what's the efficient of the treatment how you start the Dose what are the doses how you monitor them,randomization blindness is it single double triple blind what are the missions you have taken during the blinding for example you need to justify that one of the study team, they had the code for the clinical trial so in case of emergency they will inform about the treatment ,this patient is taking what is the primary secondary outcome are these Primary secondary outcomes valid outcomes for assessment might look at mortality we might look at the quality of life we might look at symptom scores or scales we need to ensure that these outcomes are also valid and appropriate ones.

sample size calculation duration follow up I need to ensure that we have enough duration follow up to get the outcomes so we need to see that authors decided that duration follow up of arm A and arm B 6 months or crossover design four months was out period and we justify the period why we have it for two weeks four weeks or six weeks based on the halflife treatment s we need to justify the duration of the follow up how many subjects completed the follow up, if you have a Dropout if you have new treatment and we have 200 patients new treatment 200 patients on taking the existing treatment for the new treatment 200 patients started you ended by 20 patients or 30 patients maybe these 170 subjects left the trial because of certain adverse reactions or they had very poor control of the disease

so we need to look at this leaving if you have a high dropout there's a question mark about this study design about the treatment itself ,these days we need to use follow what we call intention treat analysis you started with 100 patients you ended by 80 subjects will include the 20 subjects data who left the trial not the 80 who completed the study the whole 100 subjects will follow will include them in the analysis you have these 20 subjects were followed for example for two months not four months and they have these outcomes so we'll try our best to include all subjects in the study even those who left the study in the analysis, side effects very important at all visits at assessment ethical issues do you have ethical approval what are the key ethical aspects that you consider in your clinical trial analysis plan, we need to see at the Baseline that these two groups the active and control arms they are comparable there's no significant difference between them at Baseline this is very important for randomization to ensure that all subjects are having equal chance to enter the study and this will lead to the avoiding differences between the two arms at the end of the study at Baseline before the treatment any additional analysis , prognostic factors all these we have from the study then we have the conclusions so we need to consider all these aspects when we have critical appraisal of clinical trials

massage from the doc:) plz try to look at to apply these tools for surveys cross-section studies go case-control studies, clinical trials and you see that sometimes you find , large clinical trial and you can't accept the results because of certain limitations so the more you practice the critical appraisal the more you'll be able to read and apply and utilize data from Publications and also you have good skills of writing proposal manuscript because you'll avoid difference limitations of the studies so please from now on apply these tools when you write a proposal apply these tools when you write Manuscript but the key thing to apply them during The Proposal so you can avoid the limitations that can be avoidable or preventive and this switches

thank you