The Union

International Union Against
Tuberculosis and Lung Disease

OPERATIONAL RESEARCH TO IMPROVE HEALTH SERVICES:

A practical guide for protocol development, data capture and analysis, scientific writing, publishing and translation of evidence to policy and practice

**Second Edition
2024**

The Union

**International Union Against
Tuberculosis and Lung Disease**

OPERATIONAL RESEARCH TO IMPROVE HEALTH SERVICES:

A practical guide for protocol development, data capture and analysis, scientific writing, publishing and translation of evidence to policy and practice

**Second Edition
2024**

Anthony D Harries   Pruthu Thekkur

Ajay MV Kumar   Srinath Satyanarayana

Divya Nair

Contents

Tables and Figures

Tables

Figures

Preface

The Centre for Operational Research of The International Union Against Tuberculosis and Lung Disease (The Union) has for many years been a pioneer in operational research (OR) capacity building. In 2009, The Union, in collaboration with Médecins Sans Frontières-LuxOR, developed and implemented an output-oriented model of capacity building which involved 'learning by doing'. The participants were expected to learn the research skills and conduct a research study. The course consisted of three successive modules of six-seven days each interspersed over a period of 9-12 months with time-bound milestones and deliverables that participants had to achieve to remain and complete the course successfully. The model has received global recognition for its excellent outputs: approximately 90% of course participants complete the course successfully fulfilling all the milestones, including submitting a research paper for publication. Approximately 90% of these submitted papers are published. Furthermore, course alumni have self-reported that about two-thirds of all published work contributes to changes in policy and/or practice at the local, national or international level. Nearly half of the course alumni continue to undertake operational research and publish their findings after the course and they also facilitate in future operational research courses indicating impact beyond the course. This model of capacity building was adopted and adapted by the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) in 2012 as SORT IT (Structured Operational Research and Training Initiative) and it is being scaled-up globally.

While there are many teaching-learning resources, such as PowerPoint presentations, exercises, example protocols and video lectures, a written guide is currently not available. The need for a written guide has been expressed by previous course participants and facilitators. We have used the opportunity to revise and update the operational research guide developed by The Union in 2013.

Through this guide, we endeavour to

- To improve understanding of operational research in the context of public health research.
- To provide practical step-by-step guidance to develop an operational research proposal, obtain the necessary ethics approval, capture and analyse data and draft a paper for publication in peer-reviewed journals.
- To explain the process of responding to peer review with the aim of successful publication.
- To provide information about how to communicate research findings to decision makers and use local evidence to impact on policy and practice.
- To provide advice on how to embed operational research in disease control programmes within the Ministries of Health.

Authorship

International Union Against Tuberculosis and Lung Disease (The Union), Paris, France (*Anthony D Harries, Ajay MV Kumar, Divya Nair, Srinath Satyanarayana, Pruthu Thekkur*), London School of Hygiene and Tropical Medicine, London, UK (*Anthony D Harries*), Yenepoya Medical College, Yenepoya (deemed University), Mangaluru, India (*Ajay MV Kumar*).

Acknowledgements

Target audience

The target audience for this guide is professional healthcare workers who are actively engaged in implementing disease control programmes and other health services and who are interested in conducting operational research to improve health system performance and health care delivery. It particularly aims to build the skills of researchers in public health programmes, close to the supply of and demand for health services. This guide also captures the SORT IT course material in a narrative form and can act as a source for pre-course reading and post-course reference material for participants and future facilitators who are interested to replicate SORT IT courses in their settings.

Abbreviations and acronyms

AI	Artificial intelligence
AIDS	Acquired Immune Deficiency Syndrome
ANOVA	Analysis of variance
AR	Attributable risk
ARF	Attributable risk fraction
ART	Antiretroviral treatment
AUDIT	Alcohol Use Disorders Identification Test
CDC	U.S. Centers for Disease Control and Prevention
CI	Confidence intervals
CIOMS	Council for International Organizations of Medical Sciences
COREQ	Consolidated criteria for reporting qualitative research
CPT	Cotrimoxazole preventive treatment
CRF	Case report form
DOI	Digital object identifier
DMP	Data management plan
EQUATOR	Enhancing the QUAlity and Transparency Of health Research
FETP	Field epidemiology training program
FN	False negative
FP	False positive
GCP	Good clinical practice
H0	Null hypothesis
H1 (Ha)	Alternative hypothesis
HIV	Human Immunodeficiency Virus
ICMJE	International Committee of Medical Journal Editors
IEEE	Institute of Electrical and Electronics Engineers
IMRAD	Introduction Methods Results and Discussion
IQR	Interquartile range
LMIC	Low- and middle-income countries
MDR-TB	Multidrug-resistant tuberculosis
MeSH	Medical subject heading
MSF	Médecins Sans Frontières
NIH	National Institute of Health
NLM	National Library of Medicine
NTP	National Tuberculosis Programme
OR	Operational research

PCR	Polymerase chain reaction
PHCs	Primary health centres
PI	Principal investigator
PICOT	Population Intervention Control Outcome Time
PPPT	PowerPoint presentation
PR	Prevalence ratio
PTLFU	Pre-treatment loss to follow-up
QA	Quality assurance
QC	Quality control
RCT	Randomised controlled trial
RR	Risk ratio or Relative risk
SAE	Severe adverse event
SD	Standard deviation
SOPs	Standard operating procedures
SORT IT	Structured Operational Research Training Initiative
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TAT	Turn-around-time
TB	Tuberculosis
TDR	The Special Programme for Research and Training in Tropical Diseases
The Union	International Union Against Tuberculosis and Lung Disease
UK	United Kingdom
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
USA	United States of America
USD	United States Dollar
VIF	Variance inflation factor
WHO	World Health Organization

1   Introduction to operational research

This chapter introduces the definition of operational research (OR) and clarifies the various terminologies used to mean OR. It distinguishes between OR and routine monitoring and evaluation as well as other types of research, such as basic research and randomised controlled clinical trials. The chapter also provides several examples of impact of OR on changes in policy and practice, the SORT IT framework for capacity building, challenges in undertaking OR and proposes a framework for measuring the success of OR.

1.1   What is operational research?

OR has many definitions depending on the setting, discipline, the researcher and the nature of the research. The International Union Against Tuberculosis and Lung Disease (The Union) and many of its research partners define OR as follows:

"Research into strategies, interventions, tools or knowledge that can enhance the quality, coverage, effectiveness or performance of the health system or programme in which the research is being conducted." (1)

Supporting this practical definition are three basic steps to guide OR:

- Spell out well-defined goals and objectives of the health programme or system in question.

- Identify, prioritise and articulate constraints and obstacles that prevent these objectives being achieved.

- Develop research questions that address the constraints.

OR can be used to study any topic. In this guide, we will be using examples mainly from the world of tuberculosis.

1.1.1   Is OR different from implementation research and health systems research?

There are many terms used to refer to OR and these include operations research, implementation research, health services research, health systems research, effectiveness research, action research and so on. (2,3)

While one school of thought tries to differentiate between these terms, a closer look at the definitions of each of these terms indicates that there is a substantial overlap – in scope, relevance as well as characteristics – and the underlying concept is the same. Hence, we in this guide do not make any distinction between these terms and use them synonymously.

1.1.2 How is OR different from other forms of research?

There are two important differences between OR and other kinds of research. First, the research is conducted within the routine settings and not in controlled trial conditions or laboratories and second, the research is always action oriented with the intention to use the results to solve the implementation problems and make a difference to the lives of people on the ground. In this sense OR does not include basic science research or randomised controlled trials (RCT).

While efficacy (does the intervention work in ideal, controlled conditions?) is the domain of RCTs, OR deals with domains such as effectiveness (does the intervention work in routine programmatic conditions?), efficiency (can the intervention be made as effective as possible with the least use of resources such as time, personnel, materials and money?), coverage and access (whether the intervention is reaching everyone who needs it?), quality, equity and acceptability. Thus, OR comes into the picture after the efficacy of interventions has been established by RCTs. However, please note that the RCT design can be used to test for effectiveness of interventions in programmatic settings.

There is some confusion as to whether epidemiologic studies, such as tuberculosis prevalence surveys or annual risk of tuberculosis infection studies, constitute OR or not. In our view, epidemiological studies are done to understand the burden of disease in the populations and are helpful to plan for services, but they do not constitute OR.

1.1.3 Is OR a specific type of study design?

OR does not signify a particular type of study design. We may use any type of study design which is best suited to answer the research question. This can include:

- Observational study designs (which include descriptive study designs such as case series, trend analysis, ecologic studies and cross-sectional studies and analytical study designs such as cohort studies or case control studies) when we are trying to quantify the extent of the implementation gaps or quantitatively assess factors associated with the implementation problem.

- Qualitative research or mixed methods designs (which include both quantitative and qualitative research), when the objective is to identify reasons for the implementation gaps and possible solutions from the perspective of patients, providers and communities.

- Experimental study designs (such as pragmatic cluster-randomised trials) when we are trying to assess effectiveness of new interventions in real-life settings.

1.1.4 How does OR differ from using routine data for quality improvement?

At this point, it is important to make a distinction between routine monitoring and evaluation (M&E) and OR. Routine M&E is an important aspect of programme work which helps the researcher to understand whether the overall programme objectives are being achieved or not and provides information on processes helpful in programme management. But routine M&E rarely provides information on reasons for implementation gaps and possible solutions and this is where OR comes in. At the same time, high-quality surveillance data collected as part of the M&E system can be used as secondary data in some OR studies. Thus, OR and M&E are complementary to each other.

1.2 Why is OR important? Has OR been able to impact policy and practice in the past?

Despite considerable progress over the years, tuberculosis still remains the top cause of death among the infectious diseases and has devastating socio-economic consequences for people in low- and middle-income countries (LMIC). As a global community, we have committed to end the tuberculosis epidemic by 2030. An analysis of the performance of national tuberculosis programmes (NTPs) show that there are huge gaps at every step in the cascade of care of people with tuberculosis. In our view, these gaps reflect suboptimal implementation of existing strategies known to be efficacious and OR is one of the best available tools to identify the gaps and point to solutions.

OR is an essential part of the continuum of research needed to generate evidence that can be used to change policy and/or practice, scale-up implementation and eventually improve health outcomes among patients and communities.

Here are some examples from Africa and Asia to demonstrate this aspect.

- Several OR studies on HIV testing in people with presumptive tuberculosis in India led to national implementation of HIV testing and earlier initiation of antiretroviral therapy in HIV-positive people with presumptive tuberculosis. (4,5)

- OR studies conducted in Malawi on HIV testing and cotrimoxazole preventive therapy demonstrated a significantly reduced mortality in HIV-positive people with tuberculosis and this led to a national policy change of routine HIV testing and the provision of cotrimoxazole to HIV-positive people living with HIV and tuberculosis. This eventually led to improved HIV testing, improved treatment success and reduced mortality among HIV-positive people with tuberculosis. (6)

- An OR conducted in Zimbabwe led to improved scale-up of isoniazid preventive therapy in the country. (7)

Another important area where OR is used extensively is to understand 'how to' implement new tools and interventions, including recording and reporting systems to monitor their use, customised to the uniqueness of the settings in which they are to be deployed. These may include geographic areas affected by conflict (political, social or economic), environmental challenges (such as hilly terrain, marshy lands affecting access to health facilities) or unique challenges related to the health facilities itself (lack of trained human resources, limitations in infrastructure, inadequate budgets, interruptions in supplies of medicines and other consumables, suboptimal recording and reporting systems and lack of political commitment).

OR has been increasingly recognised as vital to the strengthening of health programmes. OR has been included in global plans (such as WHO's End Tuberculosis strategy) and resources have been allocated by global funding agencies, including the Global Fund to Fight against Tuberculosis, AIDS and Malaria.

1.3   Who can conduct OR?

Anyone with knowledge of research methods and programme implementation experience can carry out OR. There will be many research questions that need to be answered as countries gear up to end tuberculosis and this will not be possible with research conducted by only a few OR officers in the country. It is important to build capacity of front-line health care providers including programme managers and other professionals working in the country and expand the communities of practice. Only then, will it be possible to build a research culture within the programmes and use research as a tool to understand the reasons for the gaps in the programme and address them. Regular conduct of output-oriented capacity building initiatives, such as the Structured OR Training Initiative (SORT IT), is required for both service providers and academics to build such communities of OR practice.

1.4 What is SORT IT?

SORT IT (Structured OR Training Initiative) is a capacity building initiative. It was developed by The Union and Médecins Sans Frontières (MSF) in partnership with the Special Programme for Research and Training in Tropical Diseases (TDR). More information is available at: https://tdr.who.int/activities/sort-it-operational-research-and-training

The course consists of four successive modules of approximately six to seven days each interspersed over 9-12 months with time-bound milestones and deliverables that participants must achieve to remain in and complete the course successfully. Module 1 is on research protocol development. Module 2 is on data capture and analysis, Module 3 is on scientific manuscript writing and Module 4 is on communicating research findings.

SORT IT courses started in 2009 and, as of 31 March 2023, there had been 87 courses (some of which are still on-going) which had enrolled 1,000 participants from 94 countries around the world – more than 95% of the participants coming from LMICs.

The model has received global attention for its excellent outputs – nearly 90% of course participants complete the course successfully fulfilling all the milestones, including submitting a research paper for publication, of which nearly 90% get published. Furthermore, course alumni have self-reported that about two-thirds of all published work contributed to changes in policy and/or practice at local, national or international levels. This is encouraging and can be attributed to several factors including: policy-relevance of the research question; engagement of policy makers as co-investigators from protocol development to publication of the paper; structured, rigorous and hands- on mentorship by experienced mentors; ownership of study results especially when programme managers were principal investigators of the research project; and other windows of opportunity available to individual researchers by virtue of these individuals being in national/state level committees.

Nearly half of the course alumni continue to undertake OR and publish their findings after the course and facilitate in future OR courses, thus indicating sustained learning of skills beyond the course. This is an important indicator to show that this is a model that builds capacity which can be used independently by the course alumni.

Some of the alumni have replicated this model in their own countries, including India, Pakistan, the South Pacific region, Central Asia region and Kenya. Few capacity-building programmes track outputs and outcomes, and the SORT IT model creates a benchmark in this area. The model has also been adapted by other partners. Given the high-quality outputs of such initiatives, they deserve to be funded.

1.5 What are the challenges in undertaking OR?

While the concept of OR as an essential tool for health programmes is widely accepted, challenges to successful implementation of comprehensive OR activities at country level are numerous.

Lack of country-level political commitment: Political commitment is usually reflected in two ways: i) inclusion of OR into the national strategic plans of NTPs or other disease-control programmes and ii) having a dedicated budget line.

Inclusion of OR in the national strategic plan is important because many donors do not fund interventions which are not a part of the national strategic plans.

Dedicated budgets will be required for covering the costs of OR (salaries, travel, hotel stay during data collection visits, computers for data entry and analysis, internet, dissemination costs including publication in open access journals). Budgets for OR are frequently included under the overall M&E activity and not as a separate budget line. A major drawback of this approach is that OR does not get the required visibility and priority.

Lack of documented research priorities: Many countries still operate in the absence of a detailed, systematic research plan with clear linkages to programme priorities, thus limiting the impact of research efforts. Implementing research studies in the absence of a carefully conducted situational analysis prevents many countries from achieving their desired goals.

Lack of OR trained human resources: Having dedicated OR officers at national/ provincial level is crucial to drive the OR agenda in the countries. In addition, we need to establish communities of OR practice – both by harnessing existing capacity in academia and training service providers in OR – thus establishing collaborative mechanisms between academia and programme managers.

Lack of access to data: One of the strengths of NTPs worldwide is their excellent and structured recording and cohort reporting systems (with periodically collected follow-up data). Many countries, such as China and India, have web-based, case-based surveillance systems which capture a wealth of individual patient data. Unfortunately, such data is not fully analysed and utilised for programme decision making and one of the challenges is access to such data. This needs to change and the NTPs must make efforts to create systems and provide access to anonymised programme data to anyone who wants to analyse and make sense of it. OR studies using such data should receive expedited ethics review or a waiver of ethics review.

This will help the researchers across the country to collaborate with artificial intelligence experts to create algorithms for in-depth analysis of data and generate useful insights at frequent intervals about the programme performance and the status of the tuberculosis epidemic itself.

Lack of a forum for dissemination and fostering policy change: A disconnect between the researchers and the policy makers is one of the key challenges in the uptake and translation of evidence into policy. Most researchers think that their job ends once the research is published in a peer-reviewed journal. While this is an important milestone, it is not sufficient in case of OR studies whose goal is to inform policy/practice and improve outcomes.

Even if researchers want to engage with policy makers, they may not have access to them. To bridge this gap, we recommend that NTPs create a forum under the chairmanship of the national programme manager, which provides an opportunity for researchers across the country to share their research findings periodically (for example, once a year on a fixed day). This mechanism provides a place where researchers can directly interact with the policy makers, who can then use the latest evidence to inform policy decisions. The researchers can be asked to submit their research findings in a prescribed format well-ahead of the date of the forum and if required, there can be a process of screening by which the programme managers have an opportunity o decide which research findings get priority to be disseminated. Another option is to piggy-back on existing mechanisms, such as national tuberculosis conferences, where the NTP can dedicate an entire day for convening this forum. This model can also be applied to other health and disease control programmes.

Lack of monitoring and accountability to ensure that all OR projects reach their logical conclusion – publication, policy/practice change and improvement in outcomes.

1.6   How does one measure the success of OR?

There are three key parameters to measure the impact of OR:

- Publications
- Changes in practice and/or policy and impact on improved programme outcomes
- Capacity development of service providers and academic researchers

Figure 1.1 presents a framework that can be used for monitoring OR conducted by a disease control programme, such as NTP.

Figure 1.1 Framework to monitor operational research studies in a disease control programme

Number of OR protocols approved by
the national and sub-national committees and funded

Number of research studies completed

Number of research papers submitted to peer-reviewed journals

Number of research papers accepted for publication in peer-reviewed journals

Number of studies whose findings were disseminated to all stakeholders

Number of studies that had an impact on policy and/or practice

Number of studies that led to improved programme outcomes

1.7   When are multicentre OR studies needed?

For OR studies that are of immediate priority, we recommend that the NTP or national disease control programme leads on such studies using a nationwide, multicentre approach. This will ensure a sufficient sample size and representation of different types of contexts, so that evidence can be generalised, including context-specific variations. This type of evidence is useful when making scale-up decisions of various interventions and activities.

Following a common protocol in the different sites will enable comparison of findings across the sites. The network of OR officers in the country can be useful in coordinating such studies.

Given the ownership of the NTP in such studies, the likelihood of timely policy uptake and further implementation is high. An excellent example of such an endeavour comes from India, where an OR on screening of people with tuberculosis for diabetes mellitus in the country led to an immediate national policy decision to routinely offer diabetes testing to people with tuberculosis and subsequently widespread implementation in the country.

References

1. Zachariah R, Harries AD, Ishikawa N, et al. OR in low-income countries: what, why and how? Lancet Infect Dis. 2009; 9(11): 711-717. doi:10.1016/S1473-3099(09)70229-34.

2. WHO/TDR. Implementation research toolkit. http://adphealth.org/irtoolkit/. Accessed 9 March 2019.

3. Remme JHF, Adam T, Becerra-Posada F, et al. Defining research to improve health systems. PLoS Med. 2010; 7(11): e1001000. doi:10.1371/journal.pmed.1001000.

4. Kumar AM, Gupta D, Kumar A, et al. HIV testing among patients with presumptive tuberculosis: How do we implement in a routine programmatic setting? Results of a large OR from India. PLoS One. 2016; 11(5): e0156487. doi:10.1371/journal.pone.0156487.

5. Kumar AM, Singarajipura A, Naik B, et al. HIV-infected presumptive tuberculosis patients without tuberculosis: how many are eligible for antiretroviral therapy in Karnataka, India? J Epidemiol Glob Health. 2017; 7(1):11-19. doi:10.1016/j.jegh.2015.12.002.

6. Harries AD, Zachariah R, Chimzizi R, et al. Operational research in Malawi: making a difference with cotrimoxazole preventive therapy in patients with tuberculosis and HIV. BMC Public Health. 2011; 11(1):593. doi:10.1186/1471-2458-11-593.

7. Takarinda KC, Choto RC, Mutasa-Apollo T, et al. Scaling up isoniazid preventive therapy in Zimbabwe: has operational research influenced policy and practice? Public Health Action. 2018; 8(4):218-224. doi:10.5588/pha.18.0051.

2 Identifying and defining a research question

This chapter describes the PICOT framework for framing a research question with several examples. It also provides an outline for setting research priorities and an overall structure for an OR proposal.

2.1 How to identify and prioritise programmatic challenges that could be addressed using OR?

Identifying a research question which matches with the priority of the national programmes is key to ensuring relevance. If there is a published document with lists of national research priorities, this could guide the individual researcher to choose the OR question. If not, the best research question usually arises from problems in the routine provision of clinical and other health services. Other places for identifying a research question include listening to patient experiences during clinical practice, reading the published literature, talking to experienced colleagues and other researchers, attending conferences and thinking about questions related to the introduction of new technologies (diagnostics, drugs, vaccines, information systems) in routine health services.

At a country level, setting research priorities is one of the most important steps in steering the direction of research work related to tuberculosis or any other disease in the country. The NTP and other health and disease control programmes should explicitly list the specific research priorities so that researchers across the country work on the essential priorities of immediate policy-relevant questions rather than questions that are of academic interest only. There are some important principles to be followed in setting research priorities (Figure 2.1).

Figure 2.1 Steps to setting operational research priorities by national tuberculosis programmes (1)
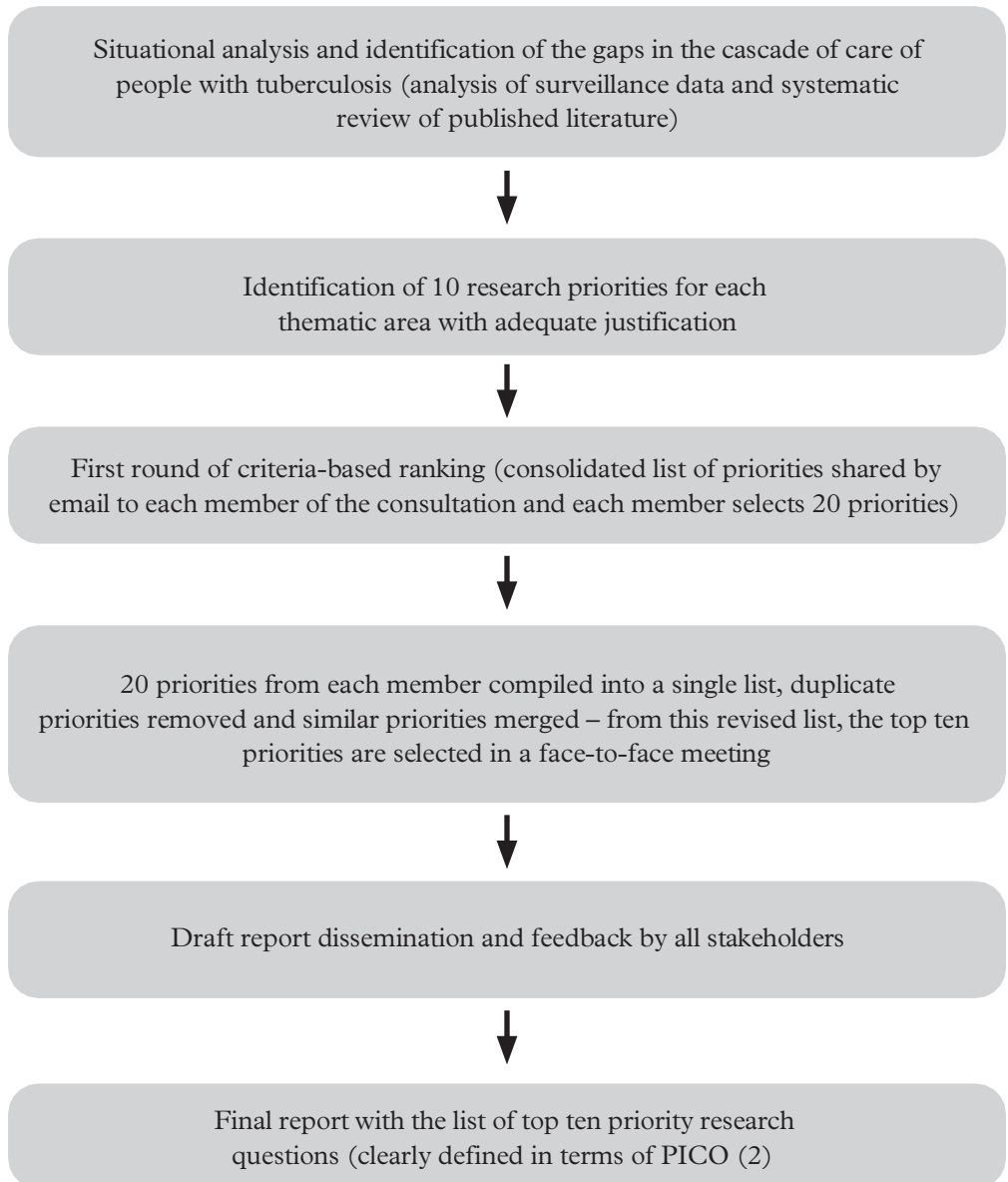
Situational analysis and identification of the gaps in the cascade of care of people with tuberculosis (analysis of surveillance data and systematic review of published literature)

↓

Identification of 10 research priorities for each thematic area with adequate justification

↓

First round of criteria-based ranking (consolidated list of priorities shared by email to each member of the consultation and each member selects 20 priorities)

↓

20 priorities from each member compiled into a single list, duplicate priorities removed and similar priorities merged – from this revised list, the top ten priorities are selected in a face-to-face meeting

↓

Draft report dissemination and feedback by all stakeholders

↓

Final report with the list of top ten priority research questions (clearly defined in terms of PICO (2)

(2) PICO=population, intervention, comparison, outcome

The first step is a detailed situational analysis of the epidemic in the country which needs to be done along with assessment of the performance of the programme against globally recommended indicators. This may be done by analysis of surveillance data as well as a systematic review of published research studies so that all the gaps in the cascade of care of people with tuberculosis are identified. This work is crucial and should be commissioned by the NTP so that the best expertise in (or outside) the country can be utilised.

Then research questions need to be framed to understand the reasons for the gaps and to assess the effectiveness of potential interventions to fill those gaps. Many documents simply list the broad areas of research rather than the specific and well-defined research priorities. The latter approach demands more work but it is preferred to guide researchers and funders.

The process should be led by a national OR officer under the chairmanship of the NTP and should involve wide consultations with stakeholders, including international technical agencies, non-governmental organisations, national research institutes, other institutions of national importance and most importantly, the civil society representatives and private providers. It is also important to include representatives of disease control programmes related to important co-morbidities associated with tuberculosis, such as HIV, diabetes and tobacco control programmes.

Ministries other than the Ministry of Health should be engaged so that OR, which is needed to develop and strengthen the implementation of the multi-sectoral accountability framework required to end TB, is undertaken.

Well known techniques such as the Delphi technique involving a multi-stage process can be used to arrive at a consensus on research priorities. It is important that the list of research priorities is sufficiently small (10-15) and well-defined, thus enabling everyone to focus on what is relevant and important rather than a long plethora of research questions.

Alternatively, one can list all the important questions and grade them by priority level. The list may be revisited periodically - we recommend at-least once every year- to include emerging research priorities. For example, in a COVID-19 pandemic situation with a disastrous impact on the health services and affecting the care of other diseases, it was important to conduct rapid OR to identify the best ways of ensuring no interruptions in the provision of tuberculosis services.

Sometimes, a question may be of local importance and not present in the list of national research priorities. This is still important and can be answered using OR.

2.2 What is the importance of having a research question?

OR, like every other type of research, must be disciplined, rigorous and precise. Sloppiness in thinking or carrying out the research is no more acceptable in OR than it is in any other type of research.

The generation of new knowledge (the intermediate goal of research) starts with a question. A clear answer to the research question enables the action needed to improve health (the end goal of the research).

K. Punch stated as follows★:

> A question well asked is a question half-answered.

The way the question (or hypothesis) is stated shows what data will be necessary to answer (or test) it and probably suggests also how and from where or from whom the data will be obtained.

2.3 How does one assess if the chosen research question is appropriate?

There are different parameters we can look at when assessing the appropriateness of a research question. They include relevance, novelty and feasibility of answering the question.

The relevance is the most important in our view from an OR perspective. Hence, it is vital that we choose a research question which is of priority to the national programmes and hence has the potential to contribute to a change in practice and/or policy.

Novelty was once considered an essential pre-requisite for publishing findings. This is no longer the case. OR may still be regarded "new" if it repeats a study in a different location or at a different time to see changes over time.

★ Introduction to social research: Quantitative and qualitative approaches, 1998, London.

Similar findings from different settings add to the consistency of association and it is thus encouraged to publish all research. Thus, novelty is not an absolute criterion, if the questions remain locally relevant.

From a practical point of view, feasibility of the research question is an important aspect to review before embarking on the research. Feasibility includes aspects such as having an adequate number of study participants, having adequate technical expertise within the research team to answer the research question and having a budget to cover the costs of conducting the OR.

2.4   How is the research question framed?

We recommend the use of the PICOT framework to frame a research question. While it is understandable that the initial question is going to be broad, it is important to focus and define the key elements in a research question and thus make it more specific. This is where a PICOT framework will help.

> PICOT is an acronym and stands for the following:
>
> P: Population/Problem (Who is the study population and what problem is being addressed? Describe by time, place and person.)
>
> I: Intervention/Exposure (What is the intervention or exposure being studied?)
>
> C: Comparison (What is the comparison group, if applicable?)
>
> O: Outcome (What is the outcome or endpoint?)
>
> T: Time period (What is the duration of the intervention or a reasonable follow-up time period in which the outcome is expected to occur? This does not refer to the calendar time when the study takes place.)

Example 1: *How do HIV-infected tuberculosis patients fare with early antiretroviral treatment (ART)?*

This is an initial broad question. Using the PICOT framework, this can be rephrased as:

Among HIV-infected tuberculosis patients, does offering early ART (in the first 2 weeks) during tuberculosis treatment improve treatment outcomes compared to late ART (after 2 months)?

Dissecting it in terms of PICOT, we get the following:

P: HIV-infected tuberculosis patients (we can make it more specific by describing time and place)

I: Early ART defined as starting ART in the first 2 weeks of initiating tuberculosis treatment

C: Late ART defined as starting ART after 2 months of initiating tuberculosis treatment

O: Tuberculosis treatment outcomes (such as cure, treatment completion, death, loss to follow-up, failure, not evaluated)

T: While this is not explicitly mentioned, this is implicit given the endpoint is assessment of tuberculosis treatment outcomes and tuberculosis treatment usually lasts for a period of 6-18 months depending on whether tuberculosis is drug-susceptible or drug-resistant.

Example 2: Here we have a broad question: Can polymerase chain reaction (PCR)assays detect tuberculosis? Rephrased, a more specific question is:

In adults with presumptive pulmonary tuberculosis, is PCR more sensitive and specific than mycobacterial culture (in liquid medium) to diagnose the disease?

Dissecting it in terms of PICOT, we get the following:

P: Adults with presumptive pulmonary tuberculosis (we can make it more specific by describing time and place and defining the age criteria of adults)

I: PCR (this is a diagnostic test and not an intervention)

C: Liquid culture

O: Sensitivity, specificity

T: There is no follow-up period because the samples are collected at one point in time and tested using both diagnostic technologies. Hence T is not relevant here.

Example 3: *In pregnant women does exposure to benzodiazepines during early pregnancy cause malformations in the newborn baby?*

Dissecting it in terms of PICOT, we get the following:

P: Pregnant women (we can make it more specific by describing time and place)

I: Exposure to benzodiazepines (this is an exposure factor and not quite an intervention)

C: No exposure to benzodiazepines (not explicitly mentioned)

O: Malformations in the newborn baby

T: While not explicitly mentioned, every pregnant woman is likely to be followed up until delivery to assess the presence or absence of malformations in the newborn baby.

Example 4: *Among HIV-infected people registered in 2014 in ART centres in Kathmandu, Nepal, what are the proportions who were screened for tuberculosis and diagnosed to have tuberculosis?*

Dissecting it in terms of PICOT, we get the following:

P: HIV-infected people registered in 2014 in ART centres of Kathmandu, Nepal (note that this is well described by time, place and person)

I: Not applicable as this is a descriptive study

C: Not applicable as this is a descriptive study

O: There are two outcome indicators being studied – proportion screened for tuberculosis and proportion diagnosed to have tuberculosis

T: Not applicable as there is no follow-up involved. Note that the calendar year 2014 mentioned above is part of the description of the population and not related to T of PICOT framework.

All the components of the framework may not be applicable in all the OR studies. For example, in a descriptive study such as the one described above, only P and O components may be applicable. In some studies, there may not be an explicit comparison group and hence C may not be applicable. Nevertheless, PICOT is a good framework to use to either develop or review an OR question.

Sometimes the population may refer to health facilities or other units of study instead of patients or people.

Example 5: *Is prolonged smear microscopy turn-around-time (TAT) in health facilities associated with a high rate of pre-treatment loss to follow-up?* Here, the P refers to the health facilities, which are a unit of study and analysis.

> Dissecting it in terms of PICOT, we get the following:
>
> P: Health facilities
>
> I: Health facilities with delay in smear microscopy turn-around-time (this is the key exposure)
>
> C: Health facilities with no delay in smear microscopy turn-around-time
>
> O: Pre-treatment loss to follow-up rate
>
> T: Not applicable as there is no follow-up involved.

Example 6: Here we have a descriptive study question: *Among patients with confirmed Ebola virus disease who received hospitalised care during 2014, what are their treatment outcomes?* Here only P and O of the PICOT are explicitly mentioned and T is implicit as end of treatment course.

Example 7: This question clarifies the T of PICOT framework: *What are the end-of-intensive phase treatment outcomes among people with multidrug-resistant tuberculosis in Belarus started on treatment from 2015 to 2019?*

In this question, T does not refer to the calendar years 2015-2019 (which is part of the description of the study population). It refers to the follow-up period of each tuberculosis patient in the study which is till the end of intensive phase of treatment.

Example 8: A qualitative research study: *What are the enablers and barriers of providing ART to HIV-infected people with tuberculosis from the perspective of people with tuberculosis, treating clinicians and programme managers?*

Dissecting it in terms of PICOT, we get the following:

P: HIV-infected people with tuberculosis,
treating clinicians, programme managers

I: Not applicable as this is a descriptive study

C: Not applicable as this is a descriptive study

O: Enablers and barriers to ART provision

T: Not applicable as there is no follow-up involved

2.5   How to prepare a concept note or application of intent?

Researchers are frequently asked to prepare a brief concept note when applying for a research grant. This is usually expected to be brief (like a one-pager) and should cover key aspects of the proposed research idea. These aspects include the background which describes the key problem that is being addressed, setting and the local epidemiology, a brief review of literature indicating what is known and what is unknown, justification or rationale for the study. This could be followed by the research question in PICOT format. A brief description of methodology, including study design, data collection, entry and analysis procedures will be needed. A description of the expected impact of the study on change in policy/practice will be a great justification for funding.

2.6   What are the components of an OR proposal/protocol?

OR studies are developed in response to a problem that stakeholders wish to address. The development of a research proposal is an iterative process that sets out to answer the following questions:

- What is the problem and why is it important to address this problem?

- What is already known about this problem?

- What does this study aim to achieve?

- How will this be achieved – what data is required and how will it be collected and analysed?

- How will the work be undertaken and what resources will be required?

The overview presented in Table 2.1 helps ensure that all the key elements required in a research proposal are addressed. The proposal should follow a logical sequence and contain sufficient information to assure health authorities, ethics review boards and donors of the need for the research, its scientific validity and the ability of the research team to implement it. It should also serve as a guide to implementation and enable other researchers to replicate the study.

Table 2.1 Overview of an operational research proposal

Title page	
	Title of the research proposal
	Investigators (full names, designations, highest qualification, email addresses)
	Affiliated institutions (including departments or faculties in universities, full postal addresses including postal/zip codes)
	Contact details (address, email, phone, fax) of the principal investigator
	Total budget requested
Introduction	
	Context
	Problem statement
	Problem analysis, including brief review of literature
	Justification and rationale
Research question	
	Research question (in PICOT format)
	Aim and objectives
Methods	
	Study setting (general and specific)
	Study design
	Study population
	Sampling, sample size
	Data variables, sources, operational definitions
	Data collection and validation procedures
	Data management (including electronic capture)
	Data analysis plan (including dummy tables and figures)
Ethics considerations	
	Review and approval from ethics review committees
	Permission to access programme data from authorities
	Consent
	Confidentiality
	Dissemination plan and stakeholder engagement
	Implications on policy and practice
Project management	
	Roles and responsibilities of investigators (study design and protocol development, data collection, data entry, data analysis, drafting the first draft of the manuscript, critical review of manuscript)
	Project timelines
	Budget
	Budget narrative
	Regulatory aspects
Appendices	
	References
	Acknowledgements
	Data collection tools (questionnaires or case report forms)
	Data dictionary (variable names, possible values of a variable, codes)

3 Developing the background, aims and objectives for an operational research proposal

This chapter provides guidance on developing the sections on background, aim and specific objectives for the OR proposal. Examples are presented. It also provides a structured framework for conducting literature search on PubMed and managing references.

3.1 How to write a background section of an OR proposal?

The introductory section of a research proposal should show that the researcher has a thorough grasp of the topic, is up to date with relevant literature and can make a compelling case for why this research is important. The approach is to start broadly with knowledge of the field of interest, narrowed to its relevance within a specific context and flowing into the problem identification, justification (which includes a review of existing literature) and research question. The introductory section of a proposal is important for stimulating the reader's interest and setting the tone for the proposal. The following structure may help in writing a coherent and strong background section.

- Setting the scene

- Specific issue of interest

- What is known and what is unknown

- Rationale and justification

Setting the scene

This involves a description of the topic of interest and its importance.

Should one define the topic being studied? It depends whether the topic being studied is a well-known one or not and it also depends on the audience. If it is a general readership, then it may be important to define the problem (for example, tuberculosis is an infectious disease caused by a bacterium, Mycobacterium tuberculosis). If the protocol (and eventually the paper) is going to be published in a Tuberculosis-specific journal, the readership is likely to be familiar with tuberculosis and it may not be necessary to define it.

To highlight the importance of the problem being studied, one can describe the problem in terms of mortality, morbidity, disability and the efforts being done to address it. When providing statistics, it is good to highlight both absolute numbers (for example, tuberculosis kills 1.6 million people every year) and relative significance (for example, tuberculosis is the second most common cause of death among infectious diseases after COVID-19).

It is prudent to begin from the global burden and then to move into the country burden ('global to local'). This could be followed by a description of the efforts being done globally to combat the problem and the progress made to date.

One of the challenges is to succinctly present information that is relevant to the problem. If the description is too long and unfocused, it may detract rather than help to frame the research problem. This section should flow naturally into the specific issue of interest.

Specific issue of interest

It is important to quickly narrow down and present the specific issue of interest within the broad problem. Continuing with the tuberculosis example: is the focus of the protocol on low case detection? Or delays in diagnosis or poor treatment outcomes? And within each specific issue identified, there may be aspects that this study is going to focus on – this needs to be described.

To get started in OR, a challenge / problem in the health system needs to be identified as a potential research domain. A problem is defined as any deviation from a norm or expected standard. If the current and desired situations in the health services can be described, the problem is usually readily identified.

The most appropriate people to identify which challenges are real and relevant are those providing health care services. Health care providers face challenges every day and most of these can become valid research questions that can be studied. The research should focus on and address challenges that are relevant to that specific location. In selecting the problem to be addressed, consider what will have the greatest impact on improving the service and on issues that could be most easily remedied.

What is known and what is unknown?

A review of literature will help in clearly delineating what is known about the specific issue being investigated and what the gaps are. The literature can include published research papers, systematic reviews, if available, as well as findings of programme reviews. If the research is aiming to address one of the gaps in knowledge, then this is already a good way of justifying why the research is needed. Sometimes, there are issues with the methodology used in previous studies or generalisability of the findings – addressing these can also be a justification for the current study.

Rationale and justification

There are many research questions which are interesting but part of putting the research into context is identifying the relevance of the problem. This can be a difficult task. Several questions can help define the need for the OR study:

- Does the knowledge to solve the challenge/problem already exist? If the knowledge exists in the country, province or clinic, then this specific challenge is not a topic for research. If the knowledge does not exist, then the topic becomes necessary. The literature review for this section should indicate what is already known in the field and what the proposed study will add to the body of knowledge.

- Does the research address a problem that represents a 'blockage' to the delivery of quality health services? Will it be possible to relieve this blockage and improve the health system using the new knowledge created by the research?

- Does the research address an issue of national priority? This is fairly easy if there are national or provincial priorities for OR but often there is not a priority list. If there is no priority list, it can be challenging to determine priorities; a starting point could be a meeting of all the relevant stakeholders to set up a priority list for OR.

- What is the potential impact of this research? Every researcher should spend time before the research starts to think through every possible outcome of the research and the impact of the results. One way of doing this is to reflect on the hypothesis and consider what the impact will be if the hypothesis is confirmed or if the hypothesis is refuted. In addition, think through the impact of the possible recommendations on the health services. It is important to think who will be affected by the research, who should act on the findings and then ensure that all these stakeholders are involved from the beginning.

Consider the following questions:

- What change may this research bring to the delivery of health services?

- Are the research findings likely to be equally effective for all people in the community – men, women, adults, children, poor, non-poor, etc.?

- What might this research change for patients?

- What concerns might health care workers have about this research and its outcome?

- What might this research change for health care workers?

- What changes to the health system might be required (e.g. to staffing, training, facilities, equipment, maintenance)?

- Will this research mean any changes to costs for the patient or health system?

- If the research is successful, which practice, guidelines or policy would need to change?

- What impact, if any, is this research likely to have on international guidelines?

Writing this section is an iterative process of identifying and thinking about a challenge in the health services, reading the literature, identifying a gap in knowledge, thinking about what this means for a specific setting, mind-mapping what is known and finally leading to asking a question.

Once the process has been completed, there should be a very clear focus for the research and this section of the proposal should be concise and reflect this focus.

3.2   How should the aims and objectives be laid out in alignment with the research question?

Once the research question is clear and defined in terms of PICOT, it is easy to develop the aim and objectives. Aim is a broad statement of the overall purpose of the research or the general intentions of the research. Objectives are specific statements with clear measurable indicators and timelines. They are nothing but research questions rephrased as statements.

Example:

Aim: To describe and quantify the gaps in the cascade of care among people with presumptive tuberculosis identified and referred by the private health care providers in Kyrgyzstan.

Objectives:

To determine among people attending private health facilities in four selected regions and the Bishkek city of Kyrgyzstan, between February 2021 and March 2022:

1. *the number of individuals screened for tuberculosis and among them, the number (proportion) identified as presumptive tuberculosis*

2. *among people with presumptive tuberculosis, the number (proportion) of people tested for tuberculosis using sputum microscopy and/or XpertMTB/RIF and the number (proportion) of people diagnosed with tuberculosis*

3. *among people diagnosed with tuberculosis, the number (proportion) started on treatment*

4.   *treatment outcomes and*

5.   *the demographic and clinical factors associated with pre-treatment loss to follow-up and unsuccessful treatment outcomes.*

Aims and objectives are usually written at the end of the background in a separate section of the protocol. However, these are summarised and integrated into the background when a manuscript is written.

3.3   How can existing literature be used to strengthen an OR proposal?

A literature review is a systematic and thorough search of the literature in order to identify as many relevant items as possible related to the subject being studied.

A literature review is not only done at the start of a proposal development, but throughout the proposal writing process, during implementation of the study itself, and when analysing and writing up the study findings. Each time a literature review is undertaken, different pieces of information are sought.

During proposal development, for example, the literature review can contribute to an understanding of the context in which the research will be undertaken, the extent of the problem and the factors influencing that problem. The literature review is essential in identifying what is already known about the problem and helps to justify the need for the proposed study. It can also assist with developing an appropriate study methodology, for example, by providing information that can be used to inform sample size calculation and by providing information on previously validated data collection tools and analytic methods.

Before starting a literature review, the researcher must have a clear idea about the content and extent of the search. There is an extraordinarily large amount of information available and therefore, one needs a specific search question to start the process. This question may be the same as the research question, but can sometimes differ, for example, when looking for background information.

There are different types of literature, including published literature, grey literature and unpublished literature. The time period for literature inclusion should be defined according to the dates when publications became available. Another consideration is the language(s) of the articles: researchers need to think carefully about the implications of omitting some languages from the search. Remember that although some articles are not written in English or a familiar language, the abstract may be available in these languages. If the abstract seems important for the literature review, the article can be translated.

Published literature can be found by searching databases, doing manual searches or contacting researchers involved in the field of interest.

Literature databases are organised in different ways and depending on the search criteria, one may choose to use primarily one type.

A database (e.g. PubMed) may be organised using a structured thesaurus with Medical Subject Headings (MeSH) terms where a keyword, abstract or author is used to identify an article of interest according to the category (or MeSH) it is ordered to. This type of a database, however, may not include the latest concepts in a field, especially in a rapidly developing science such as medicine. MeSH terms simplify the search as the indexer assigns the terms to articles dealing with similar topics. Each database is different and one has to study each one to identify how to use it efficiently and effectively.

Some researchers are inclined to use Google Scholar for literature searches. However, this is not ideal, as it does not have an in-built structure and greater thought and preparation is needed to identify keywords which incorporate all possible references. All the possible alternative descriptions of the terms have to be searched for: for example, a search for 'preventive therapy' will not identify articles with 'prophylaxis' as the key word.

Published data can also be searched manually by looking at indexing journals, abstracting journals, reference lists or library holdings at a medical library.

Contacting researchers working in the field on the topic of interest could also be considered. Names of researchers working in the field are usually available on published articles or guidelines, where the first author is often the corresponding author and an email address is supplied in the article.

Databases are also available for unpublished data. In some instances, reports (e.g. national tuberculosis programme annual reports or Global Tuberculosis Reports of World Health Organization) and conference proceedings give a good account of unpublished data. One could also consult the websites of organisations, for example, The International Union Against Tuberculosis and Lung Disease, to access the annual conference abstracts.

Grey literature, defined as "that which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers" (such as technical and statistical reports, conference proceedings, theses etc.) can be searched manually, but this is mostly done in a library and a subscription is usually needed.

Experts could also be asked to contribute, for example, with their conference abstracts.

When experts are contacted directly, it is a good idea to develop a list of questions to ensure a structured approach. It is sensible to send the questionnaire to the expert in advance to ensure that the information required is available when they are contacted.

Once a search is complete, it is crucial to record the search strategy in order to be able to replicate it in future. The following details should be recorded: date of search, data sources selected, search terms used (e.g. MeSH terms and how they are related), any limits applied, the results of the search, which abstracts were read and which articles were read, evaluated and included in the review. Remember that materials (for example, full text articles or abstracts) can be obtained on the internet (PubMed Central) or from other sources such as a medical library (with interlibrary loans) and/or reprints. Colleagues may also assist with copies of articles needed for the literature review.

The literature review needs to be specific to the research question and study. The focus areas of the review should correspond to the various aspects of the study which has been planned. Therefore, in each section of the proposal the researcher can refer to the relevant literature sources to strengthen the information presented rather than providing a 'stand-alone' literature review.

3.4   What is PubMed and what are the different principles of searching the literature in PubMed?

PubMed is a resource that most health science professionals and students search to discover published medical literature. PubMed is a database created and maintained by the National Library of Medicine, located in Bethesda, Maryland, USA. This resource has been free-of-charge since 1996 based on the decision by the Government of the United States of America, at that time.

PubMed is an index to articles published in over 5,000 biomedical journals published across the world. It covers new and old journals with a coverage of selected journals of before the 1900s.

PubMed can be searched to discover articles about the term or concept that is being considered for the research. When a "term" is searched, this generates a list of articles published in several journals. The results give "bibliographic details" about every article, including the title of the article, the names of the author(s) and also details   about the journal in which the article appears, the name of the journal, the volume number, issue number and page numbers. The articles in journals that are not yet published in the print version of journals may not include complete bibliographic details.

There are four different principles of searching in PubMed.

3.4.1 Principle 1 Word search

When PubMed is searched with a word or phrase or a sentence, the results contain the search terms in the bibliographical details of every result. The search engine retrieves results that contain words or phrases that are being searched for. Many researchers will just enter words, phrases or sentences in PubMed. For example,

- Malaria

- Retinopathy of prematurity

- Treatment of Lyme disease

And then we expect PubMed to give results about these diseases. But the search engine in PubMed is a computer's search engine and it is programmed to find and get results that contain these terms. In other words, every result will contain the search term(s) but many of the results will not be about the terms.

Look at the result below. This result shows an article that contains the phrase "Lyme disease" in the title and is obviously about Lyme disease.

Diagnosis, **treatment**, and prevention of **Lyme disease**.
Anderson RE.
JAMA. 1998 Sep 23-30;280(12):1050-1. No abstract available.
PMID: 9757845
Similar articles

Now look at the following abstract. This result shows an article that contains the phrase "Lyme disease" in the abstract, as a mention, but the article is about Bell palsy.

Am Fam Physician. 2014 Feb 1;89(3):209-12.
Common questions about Bell palsy.
Albers JR[1], Tamang S[2].
⊕ Author information

Abstract
Bell palsy is an acute affliction of the facial nerve, resulting in sudden paralysis or weakness of the muscles on one side of the face. Testing patients with unilateral facial paralysis for diabetes mellitus or Lyme disease is not routinely recommended. Patients with Lyme disease typically present with additional manifestations, such as arthritis, rash, or facial swelling. Diabetes may be a comorbidity of Bell palsy, but testing is not

3.4.2   Principle 2 MeSH search

In several electronic resources, articles are "tagged" with the right descriptors (words that describe the item). If a search is done using tags, relevant results are obtained. In PubMed, the majority of records are tagged with terms that describe the entire article. These tags are called MeSH terms. MeSH stands for Medical Subject Headings.

MeSH terms are standardised. This means that if different authors write articles about, for example, heart attacks, using different terms, such as cardiac arrest, heart arrest, heart attack etc., the indexer will still tag or describe each article with a standard term – "myocardial infarction". Each of these articles will have the term – "myocardial infarction"- in the list of MeSH terms.

A list of all standardised MeSH terms is available in the "MeSH database", which can be reached through the PubMed website. The record below shows that the title of an article gives no information about what disease(s) are covered in the article. The article has no abstract. However, the MeSH terms in the lower half of the Box show that the article is about Arbovirus infections, Asthma, Dementia and more.

The good news is that PubMed can be instructed to deliver search results that contain the requested search term(s) in the list of MeSH Terms. How is this done? If the researcher wants articles about Malaria, all that is needed is to type the word Malaria followed by [mesh]

| PubMed ▾ | Malaria[mesh] |
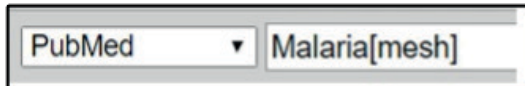
Then in the search results, every item will contain the term Malaria in the list of MeSH terms. This will happen even if the term Malaria is not present in the title or abstract.

MeSH terms are not the same as key words added in the article by the author. Neither are these terms added by the editor of the journal or the publisher. They are added to most PubMed records by "indexers" in the National Library of Medicine, USA, where PubMed is compiled and maintained.

3.4.3   Principle 3 Field search

Electronic databases are structured. Every item in a database is similar to another in structure. PubMed's items are all journal articles. So practically every item has one or more authors, a title and each is published in a journal which has a volume number, issue number and page numbers. There are some variations, but the majority are as described. Thanks to this similarity, every part of an item can be "tagged" with a "Field name". For every article item in the PubMed database, the tags are: author, title and other fields as we have just described. A simpler way of understanding this is to imagine that every record can be displayed in a table.

This is a typical PubMed record. In blue font is the title. Just below are the authors. And then the journal details: the journal name, publication year, month, volume number, issue number and page number.

Courvoisier sign.
Sonbare DJ, Sitaram V.
Natl Med J India. 2015 Mar-Apr;28(2):108. No abstract available.
PMID: 26612169
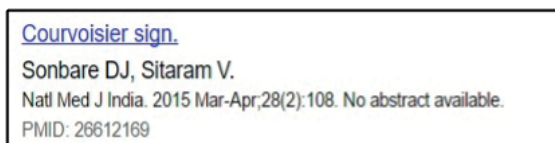
Title	Author	Journal name	Year	Volume	Issue	First page
Courvoisier sign	Sonbare Sitaram	Natl Med J India	2015	28	2	108

A search can be done with such a structure where the search term IN a specific field is specified. Let's look at the following examples.

Imaging in the **White** Dot Syndromes
Dunn JP.
Int Ophthalmol Clin. 2016 Fall;56(4):175-201.
PMID: 27575767

Alexander's disease and the story of Louise.
Wilson BA, Vargha-Khadem F, Florschutz G.
Neuropsychol Rehabil. 2016 Aug 31:1-9. [Epub ahead of print]
PMID: 27580295

In the first, the word 'White' appears in the title. But 'White' could appear as an author too. In the second, 'Wilson' is an author, but 'Wilson' is also the name of a disease. What is needed if the researcher wishes to search for the word "White" as a colour and "Wilson" as an author? This can be done by specifying that these words must be present in specific fields and this is done by adding the tags or the field names after the term.

If we type	Where the search term/s will appear in all the results
White [Ti]	White appears in the title
Wilson [AU]	Wilson will be an author

The fields are as follows:

Tag or field name to be typed after the search term	Fields
[Tiab]	Title or abstract
[JOUR]	Name of the publication
[Pdat] or [DP]	Publication date (year) or Date of publication
[Ad]	Author's address / affiliation
[Vol]	Volume number
[IP]	Issue number or part
[Page] or [PG]	Page number

Please note:

- The brackets must be square [] and not round ().

- What you type inside the square brackets is not case-sensitive.

3.4.4   Principle 4 Search using Boolean Operators

It is rare to search for a single term. If a search is carried out on a topic, several terms are usually used. To combine search terms, prepositions and conjunctions, which are used in sentences, should NOT be used. Instead, standardised terms called Boolean Operators are used.

The three Boolean Operators in PubMed are

- AND

- OR

- NOT

These must be typed in capital letters while searching.

Understanding Boolean Operators: an example

If we searched:

Let us assume we got 100 results. We now know that the results contain the word Asthma (they may or may not be about Asthma).

If we searched:

| PubMed ▼ | Asthma AND Bronchitis |

We will get <u>less than</u> 100 results because PubMed will pull out records that <u>contain both these terms together.</u>

> *Our minds are conditioned to think that 'AND' means more. We imagine that we first get 100 articles <u>about</u> Asthma and if we add AND Bronchitis, we will get additional articles <u>about</u> Bronchitis.*
>
> *We need to remember that the PubMed search engine retrieves records <u>containing both</u> terms.*
>
> *If we specify where in the record our search term should be, PubMed will retrieve records containing our terms <u>in that area</u> of the record. For example, if we search Asthma[ti] and Bronchitis[ti], we will get results that contain <u>both</u> words <u>IN the title</u> of every record.*

If we searched:

| PubMed ▼ | Asthma OR Bronchitis |

We will get <u>more than</u> 100 results because PubMed will pull out records that <u>contain at least one of the terms</u>. In other words, every record will contain either Asthma or Bronchitis or both.

> *Our minds are conditioned to think that 'OR' means only one. We imagine that we get articles about ONLY one of our search terms.*
>
> *In this case, PubMed understands that it has to give us results in which, in every record, a minimum of one of our search terms is present.*

If we searched:

| PubMed ▼ | Asthma NOT Bronchitis |

We will get <u>less than</u> 100 results because PubMed will first pull out records that <u>contain</u> Asthma. Then, <u>from the resulting set</u>, it will remove records that <u>contain</u> Bronchitis.

> *In this case, our 'normal' thinking, relating to the word NOT – works!*
> *NOT means we are eliminating something.*

The order of terms for using Boolean Operators

When "AND" is used, the order does not matter. "**Asthma AND Bronchitis**" will deliver the same number of results as Bronchitis AND Asthma. PubMed is being asked to retrieve all records that contain both terms

When "OR" is used, the order does not matter. "**Asthma OR Bronchitis**" will deliver the same number of results as Bronchitis OR Asthma. PubMed is being asked to retrieve all records that contain at least one of the terms.

When "NOT" is used, the order <u>does</u> matter. "**Asthma NOT Bronchitis**" will deliver records containing Asthma, <u>from which</u> records containing Bronchitis are removed. **"Bronchitis NOT Asthma"** will deliver records containing Bronchitis <u>from which</u> records containing Asthma are removed.

When more than two terms are used to search applying different Boolean operators, PubMed reads these terms from left to right and executes the search in that order.

For example, if the search term is "**Asthma AND Bronchitis NOT Tuberculosis**", PubMed will first deliver results where both Asthma and Bronchitis are present together. <u>From this set</u>, it will remove items where Tuberculosis is present.

But if the search term is "**Tuberculosis AND Asthma NOT Bronchitis**", PubMed will first find results where Tuberculosis and Asthma are present together. <u>From this set</u>, it will remove items where Bronchitis is present.

3.5   What is reference management and why is it needed?

It takes considerable amount of time to search for relevant literature to understand the previous body of knowledge before undertaking the proposed research work. Once the hard work of collecting the relevant literature is done, it needs to be stored in an organised manner for easy retrieval when required and for citation in a research paper or dissertation. Otherwise, time is spent unnecessarily searching for the same thing again and again. This systematic process of organising the searched literature in an easily searchable, retrievable and citable fashion is called as 'Referencing'.

'Referencing' is a system used in written work to indicate where evidence, ideas, theories, facts, or any other information, were found by providing a description of the sources. In plain English, this is a way of acknowledging the original source of information.

3.5.1 What is a reference?

Any literature that is cited and referred to in the written work to indicate the original source of the idea constitutes a 'reference' which can be any of the following.

- Scientific articles

- Books, chapters in books, atlases

- Policies, guidelines, reports

- Official sources of statistics

- Personal communication

- Unpublished documents

- Webpages, blogs

- Links to images/photographs, videos, datasets and other resources posted on data storing applications, such as Google Drive, Dropbox, etc.

3.5.2 Why should we use references?

There are many reasons for this some of which are listed below:

- To avoid plagiarism⋆ by giving credit to the original source of an idea, piece of information or resource.

- To validate and support the proposed research work with the authoritative work of another author.

- To demonstrate knowledge and familiarity with a topic and show it has been properly researched.

- To help readers find the original source of information or ideas that have been used.

⋆Plagiarism is presenting the words, ideas, data, images or media of someone else as your own without giving credit to the original source.

3.5.3   What text needs a reference in an article?

The following types of text in a OR protocol or article need a reference:

- All statements or reported data not based on the researcher's own data

- Any special methods/programmes used

- Anything that would otherwise be plagiarism

It is always a good practice to refer to the latest, the best and the most relevant reference when choosing from many. It is also advised that the author keeps a copy of all the references cited.

3.5.4   What text does not need a reference in an article?

Text that is considered common knowledge does not need a reference, such as general information which would be known by any reasonably informed member of public (for example, 'India is one of the most populous countries in the world') or specific information in a discipline which would be known by any of the researcher's peers (for example, 'Tuberculosis is a bacterial disease caused by *Mycobacterium tuberculosis*'). The results of the proposed research study and the researcher's interpretations of others' findings need not be referenced.

3.5.5   What are the different styles of referencing and is there a need for an electronic reference manager?

Acknowledging the original source of information conventionally has two components: 1) in-text citation and 2) reference list or bibliography.

In-text citation refers to the way references are cited in the main text or narrative. These may be a number (bracketed number like (1) or superscripted number like [1] or any other variation) or they may take the form of '(author-year)' depending on the style of referencing.

Bibliography is a list of all references that is inserted at the end of the written article and includes a full description of the source documents cited in the article. The list of references may be arranged in the order in which the references are cited in the text or in an alphabetical order.

There are thousands of reference styles and they can be broadly classified into three styles:

- **Numbered style**
- **Author-Date style**
- **Footnote style**

In 'Numbered style', the in-text citation is a number and the bibliography is a sequentially numbered list of references at the end of the text which provides full details of the corresponding in-text citation. Vancouver style is an example of the numbered style and is commonly used in Medicine. Other examples of numbered style include IEEE (Institute of Electrical and Electronics Engineers) style and AIP (American Institute of Physics) style.

In 'Author-Date style', the in-text citations generally include author's surname/last name along with date of publication in round brackets and the bibliography is listed at the end of the document, in alphabetical order of first author's surname/last name. Examples of author-date style include the Harvard style and APA (American Psychological Association) style.

In 'Footnote style', in-text citations are in the form of superscripted numbers and details of the reference are provided as footnotes at the end of the page. In addition, a complete list of references is provided at the end of the document, in alphabetical order of first author's surname/last name. Chicago style is an example of Footnote style.

While each journal broadly subscribes to one of these styles, they include variations of their own. Thus, it is not an exaggeration to say there are almost as many styles as there are journals and it is humanely not possible for a researcher to remember each one of these. The different styles demanded by journals, both for in-text citations and bibliographies, require significant time and attention to minute detail (including variations in bold fonts, commas, semicolons, italics, etc.) that constitute a tedious obstacle on the road to publication for all authors. Many a time, an article needs to be revised and resubmitted to another journal and this revision may involve a complete change in reference style to suit the need of the new journal.

Fortunately, there are many software programmes available for reference management such as Zotero, Mendeley, EndNote, etc. While some are free for use and distribution, others are proprietary in nature. Although the referencing software is extremely helpful, it is important to note that the electronic system used in compiling the list of references requires the correct inputs to ensure that references are in the correct format.

4   Study design, setting and study population

This chapter discusses the research terminologies that are used to describe the scientific methods adopted in OR. First, the chapter provides an overview of the study designs that are commonly used in OR. Second, it gives an outline for presenting the setting where the study is conducted. Finally, this chapter provides detailed guidance on the study reference population and sampling methods for selecting the study sample.

4.1   What are the different study designs that may be used in OR and how is the appropriate study design chosen?

4.1.1   Does OR require a different epidemiological study design?

OR can incorporate one of the epidemiological study designs and does not necessitate a distinct study design. Researchers should choose the appropriate epidemiological study designs to analyse complex health systems for optimising decision-making processes for enhancing efficiency in implementing health programmes. (1) The appropriate study design in OR is selected based on the research question to be answered and the characteristics of the data collected to answer the research question.

4.1.2   How are study designs classified?

Epidemiological study designs can be classified based on the method used to evaluate the relationship between the exposure and the outcome variable. The classification is determined by the assignment of exposure, either investigator-initiated or naturally occurring, resulting in two broad categories: experimental and observational study designs. (2) (Figure 4.1)

Experimental study designs are further categorised as randomised controlled trials (RCTs) if they involve randomisation or random allocation of study participants to intervention or the control group. (2). If this randomisation step is not employed, they are classified as non-RCTs. Observational studies, on the other hand, are classified based on the number of comparison groups. Descriptive studies have only one group, while analytical studies involve multiple groups for comparison. (3) Analytical studies further branch out depending on the approach used for the assessment of exposure and outcome as a cohort (exposure to outcome), case-control (outcome to exposure) and cross-sectional respectively (both exposure and outcome at the same time). (4)

Figure 4.1 Classification of study designs
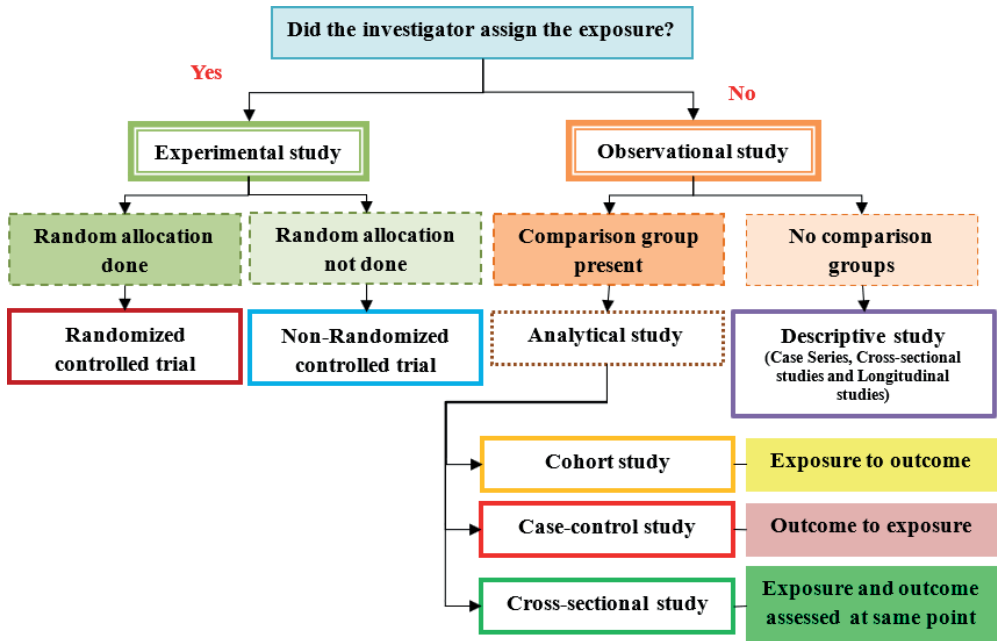
4.1.3 What factors contribute to determining the study design for conducting OR?

The study design provides a framework for carrying out the research in a systematic way to address the two essential elements of the hypothesis – the key determinant (exposure) and the outcome. (5) This emphasises the importance and usefulness of the two-by-two table at the core of the research question and hypothesis.

The first step in determining the study design can be made simply from the two-by-two table. The 'architecture' of the study (Figure 4.2) includes a 'population' that is being studied from which the individual units can be classified by the presence or absence of the key determinant/ exposure and of the outcome of interest. The figure illustrates the population, the key determinant and the outcome of interest. The final classification of the population into the four categories is found in the two-by-two table:

- Those with the determinant and the outcome of interest (a);

- Those with the determinant and without the outcome (b);

- Those without the determinant and with the outcome (c);

- Those without the determinant and without the outcome (d).

Figure 4.2 Selecting an analytical study design
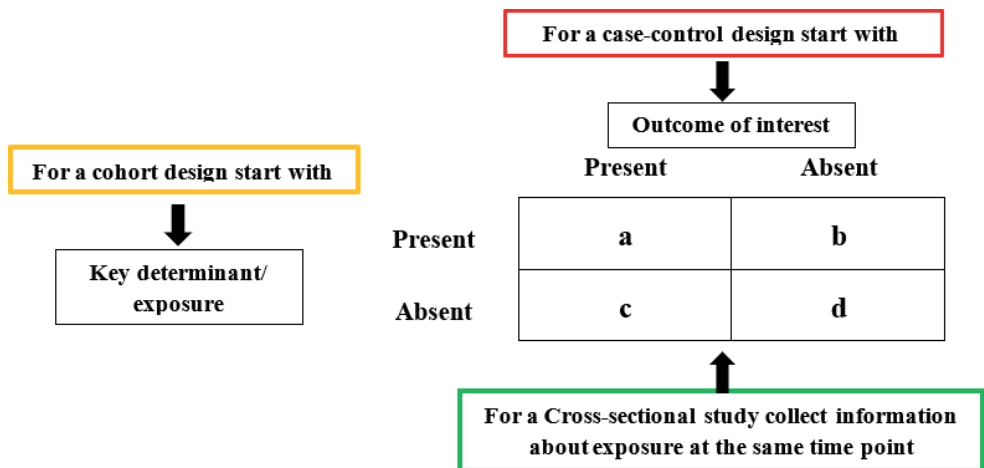
Observational study designs are most commonly adopted for OR studies. The descriptive design will have only one group and the outcomes of interest are summarised for the whole group without any comparison. In an analytical design requiring comparison across study groups, the two-by-two tables are constructed in the above fashion. Later one can decide which action was taken first: whether or not having the key determinant (enter through the 'left' of the table) or whether or not having the outcome of interest (enter through the 'top' of the table). In the former case, the study will be a cohort study design; in the latter, it is a case-control study design. In OR studies using cross-sectional design, all the information (determinant and outcome) are obtained at a same point in time and it is not known whether the determinant predated the outcome. The OR studies mainly use either cohort or cross-sectional designs and the case-control design is seldom used.

4.2   What does the cohort study design entail?

A cohort can be described as a collection of individuals who share a common characteristic. For example, a birth cohort of 2020 represents all the children born in that particular year. Cohort studies analyse the impact of exposure or determinant on the development of one or more outcomes over a duration of time without any deliberate manipulation by the researcher. The investigator first excludes the outcome of interest prior to determining the exposure. Then, the participants are divided into exposed and non-exposed groups and subsequently followed up to compare the occurrence of the outcome in both groups (incidence) over a follow-up period. (Figure 4.3)

If exposure is associated with the outcome, we would expect a proportional difference in the distribution of diseased individuals between the groups as shown in Figure 4.3.

Figure 4.3 Diagram depicting the cohort study design
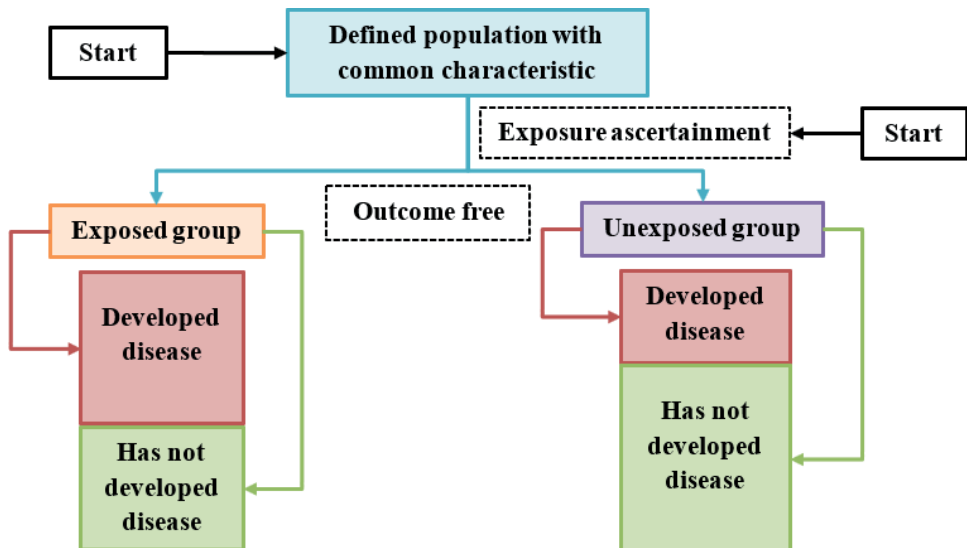
Cohort studies provide evidence of temporal relationships and yield measurements, such as incidence, relative risk (risk ratio) and attributable risk for exposed and unexposed groups.

Example: To illustrate these concepts, let us consider a scenario involving the association between smoking and lung cancer. Initially, a cohort of 20,000 individuals without lung cancer is identified and divided into two cohorts: smokers and non-smokers (10,000 in each group). Over a 10-year period, participants are followed to observe the occurrence of lung cancer and relevant data, including smoking habits, are periodically collected. In the 2x2 table below (Table 4.1), "a" (100) and "b" (9,900) represent smokers with and without lung cancer, while "c" (10) and "d" (9,990) represent non-smokers with and without lung cancer. The incidence of lung cancer among smokers is calculated as a/(a+b)=(100/10,000) and among non-smokers as c/(c+d)=(10/10,000). This indicates that out of 1,000 smokers, 10 developed lung cancer, compared to only one in the non-smoker group.

By comparing the incidence of lung cancer between the two cohorts, we can determine the risk of developing lung cancer associated with smoking. The risk ratio or relative risk (RR) is calculated as the incidence of lung cancer among smokers divided by the incidence among non-smokers:

RR = (100/10,000) / (10/10,000), indicating a tenfold higher risk of lung cancer development in smokers. Attributable risk (AR) is the risk posed by smoking after removing the background risk (i.e., the risk the individual may pose even if he/she is not a smoker).

AR = Incidence of lung cancer among smokers - Incidence of lung cancer among non-smokers

$$= 10 - 1 = 9$$

Similarly, we can calculate the attributable risk fraction (ARF), which helps to understand what proportion of the risk of developing the outcome in the exposed group is only because of the exposure.

ARF = (Incidence of lung cancer among smokers - Incidence of lung cancer among non- smokers)/ Incidence of lung cancer among smokers

$$= 10\text{-}1/10 = 90\%$$

Table 4.1 Cohort study on smoking and development of lung cancer in 10 years

	Lung cancer present	*Lung cancer absent*	*Total*
Smoker	100 (a)	9,900 (b)	**10,000**
Non-smoker	10 (c)	9,990 (d)	**10,000**
Total	**110**	**19,890**	**20,000**

4.2.1   What are the various types of cohort study designs? Are the cohort studies always prospective?

A major drawback of cohort study design is that the study population will be larger in number and needs to be followed up for a long period of time to know whether the participants develop the disease. This may also increase costs of the study. Let us consider the same example as above, supposing that we have chosen a birth cohort and about 20 years later are looking for their smoking status and then continue following the entire group to know how many of them develop lung cancer and how many do not. This will take about 40-50 years to know if smokers have a greater risk. This type of a study design is a prospective cohort study or concurrent cohort study. Adopting this study design could lead to a large attrition rate, financial issues and the participants may even outlive the investigator.

To overcome such issues other types of cohort studies can be adopted (Table 4.2). As cohort studies are forward looking, they need not always be prospective. There are retrospective and ambispective cohort studies as well. Retrospective cohort studies are those where the exposure and the outcome have already happened. The records are already available of all the individuals in the chosen cohort to know whether they have had the exposure or not and did they eventually develop the outcome or not. This kind of study is less time consuming and does not have many of the financial implications of a prospective study. However, this kind of a study may not be possible to be undertaken if the record maintenance is poor. In case of an ambispective or ambi-directional cohort study, the exposure would have happened but the outcome would not have happened yet. In ambi-directional cohort study, the exposure status of the recruited participants is extracted from the existing records and then they are followed up for a certain defined duration to determine the occurrence or not of the disease.

Table 4.2 Types of cohort study designs

Type of cohort	Time		
	Past	Present	Future
Retrospective	Exposure and outcome assessment	-	-
Ambispective	Exposure assessment	Rule out outcome	Outcome assessment
Prospective	-	Exposure assessment	Outcome assessment

Direction of enquiry and time
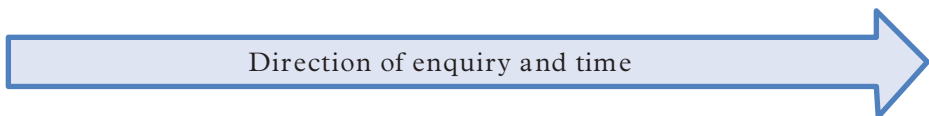
4.2.2   In what contexts can a cohort study design be adopted?

Cohort studies can generally be adopted when the exposure is rare or when multiple outcomes need to be studied. For population-based cohorts, multiple exposures and outcomes can be studied. By utilising cohort studies, researchers can establish temporal relationships and obtain precise risk estimates for the outcomes of interest.

4.3   What does a cross-sectional study entail? How do cross-sectional studies facilitate OR?

Cross-sectional studies are a type of observational research design that aims to collect data from a population at a specific point in time. In these studies, researchers gather information on a particular outcome or variable of interest from different individuals or groups within the population simultaneously. (7) The primary objective is to examine the prevalence, distribution and associations between variables at a single time point.

To better understand cross-sectional studies, let us consider an example. Suppose a group of researchers wants to investigate the prevalence of tuberculosis (active tuberculosis disease or tuberculous infection) and associated risk factors among adults in a specific community. They select a representative sample of individuals from the population and collect data during a defined period.

The researchers administer a questionnaire to the participants asking about their demographic and socioeconomic information, history of tuberculosis, contact with a person with tuberculosis and risk factors, such as, HIV infection, diabetes, tobacco smoking, alcohol use, etc. They also conduct tuberculosis investigations, such as, sputum tests, Mantoux tuberculin skin test (TST) and chest X-rays, to identify individuals with tuberculosis or tuberculous infection.

Once the data collection is complete, the researchers analyse the information to estimate the prevalence of tuberculosis in the community. They calculate the proportion of individuals with active tuberculosis, tuberculous infection or an exposure to a person with tuberculosis. Additionally, they assess the association between potential risk factors and the likelihood of having tuberculosis.

By conducting a cross-sectional study, the researchers gain insights into the burden of tuberculosis within the population at a specific point in time. They can identify high- risk groups, understand the distribution of individuals with tuberculosis and explore the relationships between risk factors and prevalence of tuberculosis. This information can help inform public health interventions and guide resource allocation for tuberculosis care and prevention.

However, it is important to note that a cross-sectional study cannot establish causality or determine the temporal sequence of events. (5) It provides a snapshot of the data, allowing researchers to describe the prevalence and potential associations between variables. To establish causality or assess temporal relationships, cohort or experimental study designs would be more appropriate.

4.4   What is a case-control study?

A case-control study is a type of observational study design used to investigate the relationship between a particular outcome (disease or condition) and potential risk factors or exposures. (8) In a case-control study, individuals with the outcome of interest (cases) are compared to individuals without the outcome (controls) to determine if there are differences in their exposure to certain factors. In a case-control study, both exposure and outcome have already happened. (Figure 4.4)

- **Selection of cases:** Individuals who have the outcome or disease of interest are identified and selected as cases. For example, if studying the relationship between nutritional status and tuberculosis, cases would be individuals diagnosed with tuberculosis.

- **Selection of controls:** A control group is chosen to represent the population from which the cases arose. Controls should be similar to cases in terms of

characteristics such as age, sex and other relevant factors, but without the outcome of interest. In the above example, controls would be individuals without tuberculosis but matched in terms of age, sex and other relevant factors. Choosing controls in a case-control study is very important. Controls can be chosen from various sources. Generally, controls will be chosen from the same hospital where the cases are chosen, from the neighbourhood where the cases are coming from or from within the close circle of family and friends of the cases. Each of the sources has its own advantages and disadvantages.

Figure 4.4 Diagram depicting the case-control study design
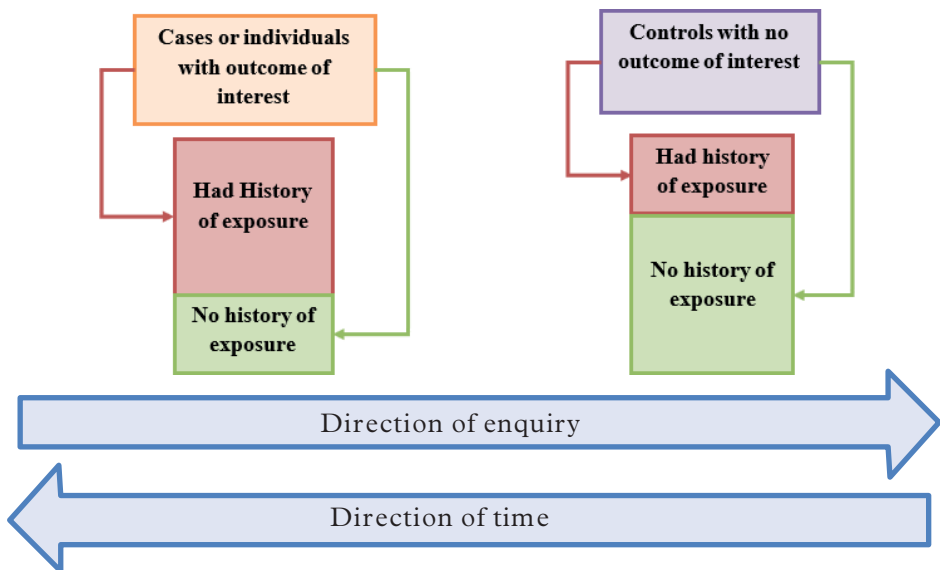
If outcome of interest is associated with the exposure, we would expect the proportional difference in distribution of exposure among diseased (cases) and non-diseased (controls).

- **Data collection:** Information is collected from both cases and controls regarding their exposure to potential risk factors. This can be done through interviews or questionnaires or record reviews.

- **Analysis:** The collected data is analysed to compare the exposure status of cases and controls. (Table 4.3) The goal is to determine if there is an association between the exposure (alcohol use) and the outcome of interest (tuberculosis). This is usually done by calculating odds ratios, which estimate the odds of exposure in cases compared to controls.

- Odds Ratio* is the ratio of odds of cases having the history of exposure to the odds of controls having the exposure. Its calculated using the formula ad/bc and hence it is also called the cross-product ratio. Let us look at the below table to understand the calculation of Odds Ratio.

Table 2.3 Case-control study on alcohol use and development of tuberculosis

	Tuberculosis present	Tuberculosis absent	Total
Alcohol use	112 (a)	176 (b)	**288**
No alcohol use	88 (c)	224 (d)	**312**
Total	**200**	**400**	**600**

Odds Ratio = (112*224)/ (176*88) = 25,088/15,488 = 1.6

The Odds Ratio of 1.6 implies that the individuals with tuberculosis had 1.6 times higher odds of having a history of alcohol use as compared to those without tuberculosis.

4.4.1   In what contexts can a case-control study design be adopted?

Case-control studies are particularly useful in situations where the outcome is rare or has a long latency period making it difficult to conduct a prospective cohort study. As this study design is adopted when the disease condition is rare, a case to control ratio can be chosen up to a maximum 1:4 to increase the power of the study.

Case-control studies can provide valuable insights into the potential causes or risk factors associated with a specific disease or outcome. However, since cases and controls are asked about the past history of exposure, there can be limitations, such as recall bias and difficulties in establishing a temporal relationship between exposure and outcome.

---

* The abbreviation 'OR' is frequently used in literature for Odds Ratio. However, we do not use it in this Guide as 'OR' is the abbreviation used for operational research.

4.5 Does OR involve only quantitative studies? Why qualitative studies are important in OR?

No, OR does not exclusively involve quantitative studies. Qualitative studies play a crucial role in OR by providing valuable insights into the lived experiences, perceptions and social contexts surrounding health-related phenomena. (9) Here is an example to illustrate the importance of qualitative studies in OR, specifically related to tuberculosis:

Quantitative aspect: A quantitative study on tuberculosis might focus on measuring the prevalence of tuberculosis in a specific population. Researchers could collect data from medical records, laboratory tests and surveys to determine the number of individuals with tuberculosis, their demographic characteristics and clinical outcomes. This quantitative study would provide statistical data on the prevalence and epidemiological aspects of tuberculosis and help identify trends and risk factors.

Qualitative aspect: However, a qualitative study conducted alongside the quantitative study would offer a deeper understanding of the social, cultural and contextual factors that influence prevention, diagnosis and treatment of tuberculosis. It could involve conducting interviews, focus group discussions or ethnographic observations with individuals with tuberculosis, healthcare providers and community members. The qualitative study could explore topics such as:

1. Perceptions of tuberculosis: Understanding how individuals perceive tuberculosis, its causes and modes of transmission within a specific cultural context.

2. Barriers to diagnosis: Identifying the challenges individuals face in seeking timely diagnosis, such as fear of stigma, lack of awareness or limited access to healthcare facilities.

3. Treatment adherence among individuals with tuberculosis. These factors could include adverse drug effects, social support or misconceptions about the duration of treatment.

4. Impact on daily life: Investigating the social and economic impact of tuberculosis on individuals with the disease and their families, including employment, income and social relationships.

By conducting qualitative research, researchers can uncover contextual nuances, personal experiences and social dynamics that quantitative data alone cannot capture. These qualitative insights can inform the development of targeted interventions and strategies to improve management of tuberculosis. For example:

- Designing culturally sensitive interventions: Qualitative findings may highlight cultural beliefs and practices that influence prevention of tuberculosis. This information can guide the development of culturally appropriate educational campaigns or interventions to address misconceptions and promote preventive measures.

- Enhancing patient-centred care: Qualitative research can shed light about treatment-related perspectives and experiences among individuals with tuberculosis. These insights can inform healthcare providers about the specific needs, concerns and barriers faced by patients leading to the delivery of more person-centred care.

- Tailoring support programmes: Qualitative studies can uncover the psychosocial, economic and practical challenges faced by individuals with tuberculosis and their families. This knowledge can guide the development of support programmes that address these specific challenges, such as providing financial assistance, counselling services or community support networks.

In summary, while quantitative studies provide statistical data on prevalence and epidemiology of tuberculosis, qualitative studies offer a deeper understanding of the lived experiences, perceptions and social contexts surrounding tuberculosis. By integrating both approaches OR can generate comprehensive insights that inform evidence-based policies, interventions and healthcare practices to effectively address the complex challenges associated with tuberculosis care and prevention.

4.6   What is a mixed method study design? What is the usefulness of conducting this kind of research?

Mixed methods study design refers to a research approach that combines both qualitative and quantitative methods within a single study. (10) This design allows researchers to gather and analyse data from multiple sources and perspectives, providing a more comprehensive understanding of the research topic. By integrating qualitative and quantitative methods, mixed methods studies can leverage the strengths of each approach to compensate for their respective limitations.

Qualitative data in mixed methods studies often involve in-depth interviews, focus group discussions, observations or textual analysis of documents. This design helps capture rich, descriptive and context-specific information, exploring the experiences perceptions and meanings attributed to a particular phenomenon. Quantitative data, on the other hand, are typically collected through structured surveys, experiments, measurements or statistical analysis of existing datasets. These methods aim to generate numerical data that can be analysed statistically to identify patterns, relationships or trends.

The integration of qualitative and quantitative data in mixed methods studies can occur at different stages, such as during data collection, analysis or interpretation. This integration allows researchers to provide a more comprehensive and nuanced understanding of the research question by triangulating multiple sources of evidence.

Mixed methods studies are particularly useful in complex research areas where a single approach may not be sufficient to capture the intricacies of the phenomenon under investigation. By combining qualitative and quantitative methods, researchers can gain a deeper understanding of the subject matter, enhance the validity and reliability of their findings and provide a more robust basis for making informed decisions or recommendations.

4.6.1   What are the types of mixed method study designs?

In health research, several types of mixed methods study designs are commonly employed to integrate qualitative and quantitative approaches. These designs allow researchers to combine the strengths of both methods, providing a more comprehensive understanding of the research question. Here are three commonly used mixed methods study designs in health research.

*   **Exploratory design:** In an exploratory sequential design, the qualitative component is conducted first to explore the research question in-depth followed by the quantitative component to further quantify and generalise the findings from the qualitative phase. The qualitative findings guide the design and development of the quantitative phase.

Example: In a study on tuberculosis treatment adherence, the qualitative phase may involve in-depth interviews with people with tuberculosis to explore their experiences, challenges and perceptions related to treatment adherence. The qualitative findings can then inform the development of a quantitative survey tool that is administered to a larger sample of tuberculosis patients to assess treatment adherence rates, factors influencing adherence and associations with treatment outcomes.

- **Concurrent design:** In a concurrent design, both qualitative and quantitative data are collected concurrently and analysed separately. The findings from each approach are then integrated and compared during the interpretation phase to gain a comprehensive understanding of the research question.

Example: A concurrent design can be applied to explore the effectiveness of a new diagnostic tool for tuberculosis. Qualitative data, such as interviews with healthcare providers, can provide insights into their experiences, perceptions and acceptance of the new tool. Simultaneously, quantitative data can be collected to measure the diagnostic accuracy and reliability of the tool. The qualitative and quantitative findings are then integrated to understand both the implementation challenges and the diagnostic performance of the new tool.

- **Explanatory design:** Explanatory mixed methods research involves collecting and analysing quantitative data followed by collecting and analysing qualitative data to further explain and explore the quantitative findings.

Example: How does the implementation of a new tuberculosis treatment protocol impact treatment outcomes and experiences among people with tuberculosis? In the quantitative phase, the researcher collects numerical data to examine the impact of the new tuberculosis treatment protocol on patient outcomes. Statistical analysis is conducted to determine the quantitative associations and patterns related to patient outcomes. The analysis shows a significant increase in treatment success rates and a decrease in relapse rates among patients following the new tuberculosis treatment protocol.

In the qualitative phase, the researcher aims to explore and explain the factors underlying the quantitative findings. They conduct interviews or focus group discussions with individuals with tuberculosis who underwent the new treatment protocol. Qualitative data collection allows them to share their experiences, perceptions and challenges related to the treatment. The researcher also interviews healthcare providers to gain insights into their perspectives on the protocol implementation. The interviews reveal that the improved treatment success rates can be attributed to the increased support and monitoring provided by healthcare providers during the treatment period. People with tuberculosis express their satisfaction with personalised care and emphasise the importance of clear communication and education about the treatment process.

Integration and explanation: The quantitative and qualitative findings are integrated to provide a comprehensive understanding of the research question. The researcher compares the quantitative data (e.g., treatment success rates) with the qualitative data (e.g., patient experiences) to explain why the new treatment protocol yielded positive outcomes. The qualitative data provide insights into patient-provider interactions, the impact of personalised care and the factors influencing treatment adherence.

By combining the quantitative findings (higher success rates) with the qualitative insights (patient experiences), the researcher can provide a more robust explanation of the impact of the new tuberculosis treatment protocol on outcomes. This explanatory mixed methods approach helps to uncover the underlying mechanisms and contextual factors that contribute to the observed quantitative results.

These mixed methods study designs allow for a comprehensive investigation of the disease, integrating qualitative and quantitative approaches to explore the experiences of tuberculosis patients, measure treatment outcomes and understand the effectiveness of diagnostic tools or interventions. The choice of design depends on the research question, the available resources and the desired depth of understanding.

4.7   How is the study setting described?

Under the study setting, the researcher needs to describe in detail the geography of the place where the study will be conducted and the existing health service delivery practice in the study site. The study setting should be described in detail to provide transparency and aid in the interpretation of generalisability of the findings. It allows readers to understand the contextual factors that may have influenced the results and helps researchers determine the applicability of their findings to other settings or populations.

The study setting can be described in two parts that are the general and specific settings.

General setting: The setting expands on the information provided in the 'context' section of the study but with a focus on where the study will be undertaken and the relevant issues in that area. Under general setting, it will be good to provide answers to the following questions:

- Which country is the study being conducted in?

- Is the country a high-income country or a low-income country?

- What are the important demographic characteristics of the population in the country?

- If the study is being implemented at the sub-national level, which state or province is the study being conducted?

- Is the selected study area primarily a rural or an urban setting?

- What is the structure of the general health system in the country or study state or province if the study is taking place at the sub-national level?

Specific setting: The specific setting should include two aspects. First, the general information about the health facilities or the community where the study is being planned. Second, the detailed description of the current standards of care for patient treatment including the recording and reporting system in the selected facilities or the community. While international standards of care have been established for many conditions (and particularly for tuberculosis), there are often local adaptations of these standards (namely, programme algorithms that are being followed, reporting systems used and the measures taken to maintain these records etc.). These all need to be described in order for those reading the findings to relate them to their own settings. For example, if the study is about tuberculosis treatment outcomes the specific setting should include answers for the following questions:

- How are people with tuberculosis diagnosed?

- How are people with tuberculosis initiated on tuberculosis treatment?

- What drug regimens are used for tuberculosis treatment?

- What adherence support mechanisms are adopted?

- How are people with tuberculosis followed-up to monitor response to treatment?

- How are tuberculosis treatment outcomes ascertained and evaluated?

- How are tuberculosis treatment outcomes recorded and reported?

- Who is responsible for each of these steps in the care of people with tuberculosis?

By reading this section another person outside the situation (in another country, in another service) should be able to understand the study setting and how it is similar or differs from their own setting. To illustrate this point, consider the difference between a study conducted in a high-income country with a low burden of HIV infection and one in a low-income country with a high HIV burden. Would the two studies (even if they addressed the same question) give exactly the same answer when it comes to the characteristics and quality of health services?

4.8 How should the study population be selected?

In OR, the selection of the study population or study sample should be in line with the study objectives. The target or reference population is the broader group to which the research findings are intended to be applied. But it may happen that we have access to only some part of this reference population. For example, the researchers plan to assess the yield of diabetes through screening of people with pulmonary tuberculosis in India but has access or permission to carry out this activity only in one or two states of the country. It follows that the researchers have access to people with pulmonary tuberculosis in only these states. The population to which the researchers have access for including them in the study is the accessible population which is a subset of the study reference population. When there is limited time and resources to include everyone from the accessible population, the researchers end up selecting and enrolling some patients into the study, which form the study sample (also referred to as study population in the protocol). The study sample is a subset of the reference or accessible population that is actually included in the research study and analysed to draw conclusions about the reference population. (11) The study sample is selected from the reference or accessible population and represents a smaller, more manageable group for data collection and analysis. To ensure that the study sample is representative of the reference or accessible population, it is crucial to employ appropriate sampling methods that maximise the possibility of selecting participants in a fair and unbiased manner.

4.8.1 What is sampling? What are the different types of sampling and their application in OR?

Sampling methods involve selecting a subset of individuals or elements from a larger population to gather data and draw conclusions. (12) These methods aim to ensure that the selected sample represents the characteristics and diversity of the entire population that the researcher wants to draw inferences about. There are two primary types of sampling methods used in OR: probability sampling and non-probability sampling. (Figure 4.5)

Figure 4.5 Types of sampling method
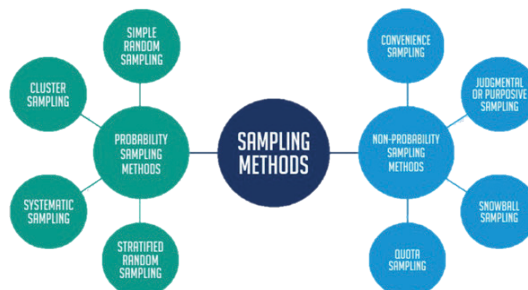
Probability sampling: Probability sampling involves random selection, providing each element in the population with a known and non-zero chance of being included in the sample. This method allows researchers to make strong statistical inferences about the whole population based on the sample. Some commonly used probability sampling methods include:

- **Simple random sampling:** In this method, each individual or element in the population has an equal chance of being selected. For example, if a researcher wants to estimate the prevalence of presumptive tuberculosis in a selected community where the line list of all individuals is available, the participant is chosen either by a lottery method or by using a random number generator to select the required number of participants.

- **Systematic sampling:** Systematic sampling involves selecting every nth participant from the population after randomly choosing the first participant. Systematic sampling can be used when the researcher has access to a list of the entire population or when he/she is unable to access a population list in advance.

  Example: Let us assume we want to study the prevalence of tuberculosis in a city with a population of 10,000 individuals.

  Step 1: Define the population: The population in this case is the entire city population of 10,000 individuals.

  Step 2: Decide on the sample size: a sample size of 500 individuals is required to represent the population.

  Step 3: Calculate the sampling interval (k): The sampling interval (k) is determined by dividing the population size by the desired sample size. In this case, k = 10,000 / 500 = 20. So, we need to select every 20th individual from the population.

  Step 4: Select the sample and collect data: To select the sample, we randomly choose a number between 1 and 20 as the starting point. Let us assume we randomly select the number 7. We would then select the 7th individual from the population and subsequently, every 20th individual thereafter until we reach a total sample size of 500.

- **Stratified Sampling:** Stratified sampling involves dividing the population into homogeneous groups or strata based on certain characteristics (e.g., age, gender, location) and then selecting a proportionate or disproportionate sample from each stratum. This ensures representation from each sub-group of the population.

    Example: Let us hypothesise that the prevalence of presumptive tuberculosis is higher in urban slums as compared to the rural population as it could be a known confounder that could make the difference. Assuming that the proportion of urban/ rural in the selected state is 70:30, then we choose 70% of samples from urban and 30% of samples from rural groups or strata in the case of proportionate sampling. In disproportionate stratified sampling, the sampling fractions assigned to each stratum are set to be unequal. This means that some strata are given a higher probability of being selected in the sample, while others have a lower probability. This can be adjusted by giving weightage during the time of analysis.

- **Cluster Sampling:** Cluster sampling is commonly used to study large, dispersed populations. It involves dividing the population into clusters or groups, randomly selecting some clusters and including all elements within the selected clusters in the sample. This method is useful when it is difficult to access individuals directly, such as surveying students in different schools or patients in different hospitals.

    Example: A newly developed artificial intelligence (AI)-assisted diagnostic tool in diagnosing tuberculosis is introduced in some of the primary health centres (PHCs) as an intervention. The PHCs are considered clusters and these clusters are chosen randomly and the tool is used in diagnosing all the patients in the cluster. The yield of diagnosis is checked between the clusters with the AI tool and those without the AI tool. Here, it is hard to implement the intervention in all the peripheral settings. In these situations, cluster sampling helps to reduce the cost, time and logistic challenges.

Non-probability sampling: Non-probability sampling methods involve non-random selection and do not provide each element in the population with a known chance of being included in the sample. These methods are often used when it is not feasible or practical to use probability sampling. However, non- probability sampling may introduce bias and limit the generalisability of the findings. Some examples of non-probability sampling methods include:

- **Convenience sampling:** Convenience sampling involves selecting individuals who are readily available or easily accessible. This method is commonly used for quick and convenient data collection but it may introduce bias because the sample may not represent the entire population.

- **Purposive sampling:** Purposive sampling involves selecting individuals who meet specific criteria relevant to the research question. Researchers intentionally choose participants who can provide valuable insights or represent certain characteristics of interest. It is the most common technique used for choosing participants for the qualitative component of the study.

- **Snowball sampling:** Snowball sampling involves initially selecting a few individuals who meet the research criteria and then asking them to refer or recruit additional participants. This method is useful when studying hidden or hard-to-reach populations.

- **Quota sampling:** Participants are selected based on predetermined quotas for certain characteristics. It ensures the representation of specific sub-groups in the sample but may introduce biases due to non-random selection. Findings may not be generalisable to the entire population.

It is important for researchers to clearly explain the sampling method used in their research to ensure transparency and validity of their results. Additionally, they should address potential biases and limitations associated with their sampling approach.

4.9   How is the study period defined?

In OR the study period refers to the specific duration or time frame during which the study will be conducted. It is from the time of conceptualisation of the study until its completion including report submission. It represents the temporal scope of the study and influences the planning, execution and interpretation of the research findings. The study period is determined based on the research objectives, available resources and practical constraints. It may be defined in terms of days, weeks, months, or even years, depending on the nature and complexity of the research question. The study period extends to the time required for data cleaning, coding, entry and analysis. It also includes the time needed for preparing research reports, manuscripts, or presentations for dissemination.

Study reference period: The study reference period encompasses the time period during which the study participants are included in the study. In a cross-sectional study involving primary data collection, the study reference period is the time period during which the participants are contacted and the data is collected. For example, in June 2023, a cross-sectional analytical study was planned to assess the association between gender and depression in a city X and researchers decided to collect data during August to December 2023. Thus, all those individuals available during August to December 2023 will be included and it forms the study reference period.

In cohort and in cross-sectional studies with secondary data extraction from the existing records, the study reference period refers to the time period during which the participants are included. For example, in June 2023, a cohort study was planned to assess the difference in tuberculosis treatment outcomes among males and females and it was decided to include all individuals with tuberculosis initiated on treatment from January to December 2022. The time period of January to December 2022 is the study reference period.

Data collection period: This refers to the period when the data will be collected. The data collection period should be carefully planned to ensure adequate coverage of the research variables and to minimise bias. As discussed earlier, in cross-sectional studies with primary data collection, it is the time period when the researchers reach out to study participants and collect data. Whereas, in cohort studies, it is the period when the data will be collected and it can be different from the study reference period. For example, in June 2023, a cohort study was planned to assess the difference in tuberculosis treatment outcomes among males and females and it was decided to include all the tuberculosis patients initiated on tuberculosis treatment during January to December 2022. The researcher extracts data during the period from August to December 2023.

Intervention or treatment period: In some OR studies, there may be an intervention or treatment administered to evaluate its impact. The study period would include the duration of the intervention during which data is collected before, during and after the intervention to assess its effectiveness. For example, a study evaluating a new intervention for improving the nutritional status of individuals with tuberculosis may involve pre-intervention assessments, the intervention period and post-intervention evaluations.

4.10   How is sample size calculated in OR studies?

Sample size calculations indicate the smallest number of research participants (facilities, individuals) required based on the assumptions used. (13) Determining the appropriate sample size is crucial in OR studies, as it ensures that statistically valid conclusions can be drawn. Since it is often impractical to include the entire target population, a representative sample is selected. Where the **sample size is too small**, the **results may be inconclusive** (the observed difference between the study groups is too small to conclude that it is statistically significant) or imprecise (the confidence limits are too wide). The time, effort and resources put into the study will have been wasted. Wastage may similarly occur if a larger than required sample size is used.

The calculation of sample size depends on several factors, including the study design, level of significance, power required, anticipated outcomes and the magnitude of the difference to be detected.

By convention most studies set the **level of significance** (α) at 5%. This is the probability of incorrectly rejecting the 'null' hypothesis (statement of no association): i.e. there is a 5% probability of rejecting the statement 'there is no difference between the study groups' when there is in fact no difference. (14)

The **power** (1- β) required is set at 80%. β is the probability of incorrectly accepting the null hypothesis i.e. accepting the statement of no association between the groups when in fact a difference really exists between the groups in the target population. (14)

The **anticipated outcomes** in the groups require an estimation of the proportion (%) unexposed with the outcome ('c' in the two-by-two table) and either the proportion (%) exposed with the outcome ('a' in the two-by-two table) or the Odds Ratio.

Estimating the anticipated outcomes in the groups is often frustrating for the researcher who has never done it before. The question posed is 'If I knew the answer to this, why do I need to do the study?' Whilst the precise levels are not known and will be determined by the study, reasonable estimates can be made based either on findings from other similar research studies or from routine data. Reviewing the literature from other studies that have looked at the problem allows the researcher to use the frequencies that have been reported in those studies as the basis for these estimates. Frequencies reported in routine data can also help with these estimates.

To calculate the sample size for prevalence studies in OR using OpenEpi software (15) follow these steps:

1. Open OpenEpi software and select "Sample Size" from the menu bar.

2. Choose the calculation for proportion.

3. Enter the following parameters:

    • Anticipated percentage frequency: This is prevalence (as percentage) of the outcome of interest that we anticipate in our study. This anticipated prevalence is either an informed estimate based on the previous literature or a guesstimate based on the subject knowledge.

    • Confidence limit or absolute precision: This is the measure of extent of sampling error that the researcher is ready to allow. For example, the anticipated prevalence is 50% and the researcher includes an absolute precision of 5%, the 95% Confidence Interval for the prevalence of 50% would be 45% to 55%. It is important to note that the absolute precision should not be more than 20% of the anticipated prevalence. For example, if the anticipated prevalence is 40%, the researchers should not take an absolute precision of more than 8%.

    • Design effect of 1: If simple random sampling is included, then the design effect should remain as 1. If the cluster sampling or multi-stage sampling is considered, the design effect would be greater than 1. In such cases, consult a statistician to decide on the design effect.

4. Click "Calculate" to obtain the various sample size calculations.

Example: Let us say we want to calculate the sample size for a cross-sectional study to estimate the prevalence of depression. Based on the previous literature, we assume the prevalence of depression in our study setting to be 50%. The researcher decides to take 5% of absolute precision for calculating the sample size at the 95% confidence limit. The design effect is 1, as the researcher adopts a simple random sampling technique for selection of participants. Using OpenEpi software with the provided parameters, we get a sample size of 384 individuals.

For OR studies estimating the incidence (follow-up) of the disease of interest, the calculation of sample size is similar to that of studies assessing prevalence. Follow the same steps as mentioned earlier. However, additional adjustment that may be required for follow-up studies to account for any possible attrition from the study cohort.

Example: Let us say we want to calculate the sample size for a longitudinal descriptive study to estimate the incidence of depression among adults over one year. The researcher wants to include individuals without depression and later reassess them for depression at the end of one year. Based on the previous literature, the researcher assumes the incidence of depression in the study setting over one year to be 10%. The researcher decides to take 2% of absolute precision for calculating the sample size at the 95% confidence limit. The design effect is 1, as the researcher adopts a simple random sampling technique for selection of participants. On calculation of sample size using the OpenEpi software, the minimum sample size required is 864 individuals. If there is a possibility of 10% attrition from the study cohort, then the researcher needs to account for this attrition. To have 864 individuals for assessment at the end of the study, the researcher has to include 960 (864 × 100/90) individuals.

For cohort studies:

To calculate the sample size for cohort studies using OpenEpi software follow these steps:

1. Open OpenEpi software and select "Sample Size" from the menu bar.

2. Choose the calculation for Cohort/RCT studies.

3. Enter the following parameters:

    •   Two-sided confidence level (1-α) at 95%.

    •   Power (1-β) at 80%.

    •   Ratio of unexposed to exposed in the sample as 1 (unless there are limited numbers of exposed, in which case use a higher ratio to increase the power of the study).

    •   Percent of unexposed with the outcome: This is the incidence (in percentage) of the outcome of interest that is anticipated among those without the exposure. This anticipated incidence is either an informed estimate based on the previous literature or a guesstimate based on the subject knowledge.

    •   Include one of these parameters: The Odds Ratio or the percent of exposed with the outcome or risk/prevalence ratio or risk/prevalence difference: This also based on either the previous literature or a guesstimate based on the subject knowledge.

4. Click "Calculate" to obtain the various sample size calculations.

Example: Let us say we want to calculate the sample size for a cohort study to assess the association of gender with risk of developing depression among adults over one year. The researcher wants to include adult males and females without depression and later reassess them for depression at the end of one year. Based on the previous literature, the incidence of depression among males is estimated at 10% and among females at 15%. The researcher decides to take males and females at ratio of 1:1 and assumes a two-sided confidence level of 95% and power of 80%. On calculation of sample size using the OpenEpi software, the minimum sample size required is 722 males and 722 females.

If there is a possibility of 10% attrition from the study cohort, then the researcher needs to account for this attrition. To be able to have 722 males and females for assessment at the end of the study, the researcher has to include 803 ($722 \times 100/90$) males and females.

The sample size for the cross-sectional analytical studies can be calculated using Cohort/RCT option under the Sample Size option in the OpenEpi software.

4.11   What are operational definitions?

Operational definitions are used to describe how a particular variable will be measured and interpreted in a study. This is often decided by the investigator based on his/her subject knowledge or with the help of a literature review. Operational definitions play a crucial role in ensuring consistency and comparability of findings across different studies. They help researchers define and measure variables in a precise and replicable manner, facilitate the evaluation of interventions, monitor disease trends and inform policy and clinical decisions.

Suppose the research study aims to investigate the 'treatment success rate' among people with tuberculosis, it is important to provide an operational definition for 'treatment success'. For example, the programmatic tuberculosis treatment outcomes include cured, treatment completed, death, lost to follow-up, treatment failure and not evaluated. In this case, the researchers have to provide an operational definition for the 'treatment success' in the research protocol. It can be mentioned that the 'treatment success' is defined as those with ascertained outcomes of either cured or treatment completed.

By employing this operational definition, the researchers ensure a standardised and measurable assessment. It specifies the key components of the outcome and provides clear criteria for classifying or calculating the outcome of interest.

References

1. Zachariah R, Harries AD, Ishikawa N, et al. Operational research in low-income countries: what, why and how? Lancet Infect Dis. 2009; 9(11):711–7.

2. Celentano DD, Szklo M, Gordis L. Assessing Preventive and Therapeutic Measures: Randomized Trials. In: Gordis Epidemiology. 6th Edition. Philadelphia, PA, 2018: Elsevier; 2018.

3. Grimes DA, Schulz KF. Descriptive studies: What they can and cannot do. Lancet. 2002; 359(9301):145–9.

4. Grimes DA, Schulz KF. An overview of clinical research: The lay of the land. Lancet. 2002; 359(9300):57–61.

5. Grimes DA, Schulz KF. Bias and causal associations in observational research. Lancet. 2002; 359(9302):248–52.

6. Grimes DA, Schulz KF. Cohort studies: Marching towards outcomes. Lancet. 2002; 359(9303):341–5.

7. Celentano DD, Szklo M, Gordis L. Cross-Sectional Studies. In: Gordis Epidemiology. 6th Edition. Philadelphia, PA, 2018: Elsevier; 2018.

8. Schulz KF, Grimes DA. Case-control studies: Research in reverse. Lancet. 2002; 359(9304):431–4.

9. Sofaer S. Qualitative methods: what are they and why use them? Health Serv Res. 1999; 34(5 Pt 2):1101.

10. Creswell J, Plano Clark V. Designing and Conducting Mixed Methods Research. Second. London (United Kingdom): Sage Publications Ltd; 2010. 142–5.

11. Banerjee A, Chaudhury S. Statistics without tears: Populations and samples. Ind Psychiatry J. 2010; 19(1):65.

12. Setia M. Methodology Series Module 5: Sampling Strategies. Indian J Dermatol. 2016; 61(5):505–9.

13. Martínez-Mesa J, González-Chica DA, Bastos JL, et al after Bastos JL. Sample size: how many participants do I need in my research? An Bras Dermatol. 2014; 89(4):609.

14. Shreffler J, Huecker MR. Hypothesis Testing, P Values, Confidence Intervals and Significance. StatPearls 2023.

15. Dean A, Sullivan K, Soe M. OpenEpi: Open Source Epidemiologic Statistics for Public Health [Internet]. OpenEpi. 2023 [accessed 25 August 2023]. Available from: https://www.openepi.com/Menu/OE_Menu.htm.

5 Ethical considerations

This chapter describes an overview of the ethical considerations in OR and provides models for preparing an informed consent form.

5.1 What are the ethical considerations relevant to OR and how can these be addressed?

Overall, the word "ethical" means being right, fair, decent, just. The primary purpose of ethical considerations is to safeguard the dignity, rights, safety and well-being of research participants. Ethical considerations in OR involve the application of ethical principles in designing and implementing research and in the usage of the research outputs. Ethical considerations also help in preventing scientific abuse and misconduct and in regulating the research activities.

The goal of OR is to develop generalisable knowledge that improves human health through better implementation of public health interventions. In the process of generating knowledge, OR studies may involve collecting data from human participants or health systems. For example, to know the effectiveness of a new drug or treatment strategy for a disease under routine programmatic conditions OR may involve observing people on various drugs or treatment strategies. This may entail benefits for most people but risk of harm to some people (e.g., adverse drug reactions). OR has the potential to exploit this situation. The purpose of ethical guidelines is both to protect patients and/or the health systems from harm and to preserve the integrity of the science.

The ethical guidelines in place today are due to past abuses, the most notorious of which were the experiments conducted by Nazi's during the Second World War (1) or the experiment in Tuskegee, Alabama, USA, in which treatment was withheld from 400 African American men with syphilis so that scientists could study the natural course of the disease. (2) Various ethical guidelines were developed in the 20th century in response to such studies. These have been described as 25 guidelines in the "International Ethical Guidelines for Health-related Research Involving Humans". (3) Though all these 25 guidelines are important, the following seven principles are relevant for OR (4):

- Social, clinical and/or public health value
- Scientific validity
- Favourable risk-benefit ratio
- Fair subject selection
- Independent review

- Informed consent
- Respect for potential and enrolled subjects.

Social, clinical and public health value

Every OR study is designed to answer a specific research question. The research question and answer should be important enough to justify the resources spent in conducting the study or asking people to accept some risk or inconvenience for participating in the research. In other words, answers to the research question should contribute to scientific or public health understanding of health or improve our ways of preventing, treating or caring for people with a given disease to justify exposing participants to any kind of risk or the burden of research. The justification for conducting the OR study should be reflected in the protocol. Any study that is "unjustified" is "unethical" to conduct.

Scientific validity

A study should employ the most appropriate methods that will answer a research question. This includes considering whether the question asked is answerable, whether the research methods are valid and feasible and whether the study is designed with accepted principles, clear methods and reliable practices. Research conducted using inappropriate or inadequate methods is unethical because it is a waste of resources and exposes people to risk for no purpose.

Favourable risk-benefit ratio

No research is risk free. There is inherent uncertainty about the degree of risks and benefits associated with an OR study. Risks may be trivial or serious, transient or long-term. Risks can be physical, psychological, economic, or social. Everything should be done to minimise the risks and inconvenience to research participants to maximise the potential benefits and to determine that the potential benefits are proportionate to, or outweigh, the risks. All potential serious adverse events pertaining to the OR study procedures must be identified and a mechanism should be in place to ascertain and report on these adverse events.

Fair subject selection

The recruitment of participants in an OR study should be based on the public health goals of the study and may include vulnerable populations. Participants who accept the risks of research should be able to enjoy its benefits (as far as possible). If specific vulnerable groups, such as pregnant women or children, are included as research participants, then there must be adequate justification for including them into the study and all efforts should be made to minimise any risks or harms.

Independent review

To minimise potential conflicts of interest and make sure a study is ethically acceptable before it starts, an independent ethics review panel should review the proposal and ask important questions, including: Are those conducting the trial sufficiently free of conflict of interests? Is the study doing all it can to protect research participants? Has the study been ethically designed and is the risk–benefit ratio favourable?

Informed consent

Potential research participants should make their own decision about whether they want to participate or continue participating in research. This is done through a process of informed consent in which individuals:

- Are accurately informed of the purpose, methods, risks, benefits and alternatives to the research

- Understand this information and how it relates to their own clinical situation or interests

- Make a voluntary decision about whether to participate. A model information and consent sheet are provided in Appendices 1 and 2.

Respect for potential and enrolled participants

Individuals should be treated with respect from the time they are approached for possible participation to the end of their participation, even if they refuse enrolment in a study, and after their participation ends. This includes:

- Respecting their privacy and keeping their data/private information confidential

- Respecting their right to change their mind, to decide that the research does not match their interests and to withdraw without a penalty

- Informing them of new information that might emerge during research which might change their assessment of the risks and benefits of participating

- Monitoring their welfare and, if they experience adverse reactions, unexpected effects, or changes in clinical status, ensuring appropriate treatment and, when necessary, removal from the study

- Informing them about what was learned from the research.

5.2   Is ethical approval mandatory prior to embarking on OR?

Any research involving data collected from humans (directly or indirectly) requires ethical approval. Exceptions include secondary analysis of publicly available anonymised individual patient data, aggregate data or reports. Systematic reviews and/or meta-analysis of studies that have been published also do not require ethical approval. When in doubt it is always better to approach an ethics committee to seek their opinion on whether ethical approval is needed or not. One of the other most important aspects in multi-institution and/or multi-country OR studies is that ethics approval will be needed from each of the participating institutions' committees and from a recognised national ethics committee from each of the participating countries.

Depending upon whether the OR involves primary data collection or use of existing data, the ethics committee may decide whether the research requires expedited review or full ethics committee review. In general (but not necessarily), ethics committees may adopt the following procedures for review of the operational research proposals that are submitted to them (Figure 5.1).

Figure 5.1 Procedures for reviewing operational research protocols
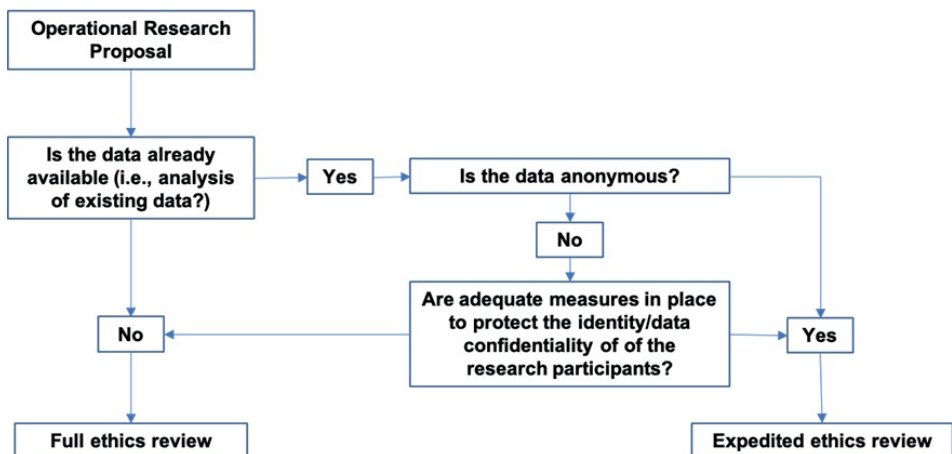
Researchers must be aware of these procedures that may be adopted by the ethics committees and indicate these issues to the ethics committee. The final decision to go for an expedited review or a full ethics review lies with the ethics committee.

5.3   What does the process of applying for ethical approval entail?

Many ethics committees specify an application form through which researchers apply for ethical approval. These application forms require researchers to provide a justification for undertaking the research in terms of the scientific and societal value of a particular research, the names and profiles of the researchers and their institutions, the research questions that are being answered, the methods that are being employed to collect the data, the risks and benefits for the participants of research and how the research participants are protected from harms, data confidentiality issues, funding sources for the research and conflicts of interest. The ethics committee may have members who are non-technical. Therefore, it is expected that the ethics application form is written in plain language without technical jargon (in a language that can be understood by members without any a priori subject matter experience in the field).

In addition to the application form, researchers are expected to submit the following documents for ethics review:

- Complete research protocol

- Participant information sheets and consent forms (if applicable)

- Questionnaires or interview guides (if applicable)

- Brief CV for the principal investigator and other investigators

- Serious adverse event (SAE) reporting form

Additional documents (such as conflict-of-interest declaration forms) may be required. Researchers must make sure that they submit all the 'mandatory' documents.

After submission, the ethics committee may take a few days to a few months to review the proposal and other documents and give approval. The ethics committee may seek clarification or may have some suggestions to modify the protocol. Researchers must address these point-by-point and incorporate all the suggestions received from the ethics committees.

Are there any guidelines or country specific resources that may be useful while applying for ethics approval for OR?

Some of the influential codes of ethics and regulations at the global level that guide ethical clinical research include the following (as referenced in the list on page 72):

- Nuremberg Code (1947) (5)

- Belmont Report (1979) (6)

- Declaration of Helsinki (2000) (7)

- International Ethical Guidelines for Health-Related Research Involving Humans (latest version 2016) (3)

At the individual country level, there may be national guidelines for the conduct of research. It is the responsibility of the study investigators to be aware of and adhere to the national and international ethics guidelines.

5.4   How are ethical considerations presented in the OR proposal?

There should be a separate sub-section on ethics issues in an OR protocol under the methods section. In this section, the information about/name of the ethics committee that will be reviewing the proposal must be clearly mentioned. Information whether consent will be obtained should be clearly specified and if informed consent is being obtained, the information and consent sheet should be provided as appendices to the OR protocol. If information and consent is given in the local language, then the translated versions of the information and consent sheet must be provided.

References

1. United States Holocaust Memorial Museum. Nazi medical experiments. Available: https://encyclopedia.ushmm.org/content/en/article/nazi-medical-experiments, accessed 24 August 2023.

2. Alsan M, Wanamaker M. Tuskegee and the health of black men. Q J Econ. 2018; 133: 407–455. doi:10.1093/qje/qjx029.

3. Council for International Organizations of Medical Sciences (CIOMS). International ethical guidelines for health-related research involving humans, Fourth Edition. Geneva, Switzerland; 2016. Available: https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf, accessed 24 August 2023.

4. National Institutes of Health. Guiding principles for ethical research. Available: https://www.nih.gov/health-information/nih-clinical-research-trials-you/guiding-principles-ethical-research, accessed 24 August 2023.

5. Shuster E. Fifty years later: the significance of the Nuremberg Code. N Engl J Med. 1997; 337: 1436–40. doi:10.1056/NEJM199711133372006.

6. United States Department of Health and Human Services. The Belmont report. 1979. Available: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html, accessed 24 August 2023.

7. World Medical Association. WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects. Available: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/, accessed 24 August 2023.

6 Project management

This chapter describes the project management aspects of the planning and implementation of an OR study which includes developing SOPs, training materials, pilot testing and budget considerations.

6.1   What are the considerations in preparing a field plan for OR?

Most operational researchers work in five phases. When the researcher completes each of these phases effectively, it increases the chances of a positive outcome with project objectives. The five phases of an OR project are: protocol development (and obtaining ethics and administrative approvals); implementation planning; execution; monitoring/ quality assurance; and closing. In each of these five project management phases, OR teams must follow a structured approach to ensure that the OR project closes according to schedule, budget and scope.

The operational researchers should decide a-priori who, what, when, where and how a project will be implemented. All risks and challenges must be identified and contingency plans should be put in place to minimise the risks and/or address the challenges.

Protocol development

During the first phase of a project, the research team develops the protocol, usually with input from all stakeholders. Important parts of this phase include defining the problem statement or purpose of the OR project and setting a scope for the project. The protocol development phase sets the stage for ongoing project performance. Ethics and other administrative approvals must be obtained at this phase before the operational researcher proceeds to the next step. Securing the budget required to complete the OR study is also done during this phase.

Implementation planning, including SOP development, training and piloting

In the implementation planning phase, operational researchers work to create standard operating procedures (SOPs) taking into consideration a reasonable project schedule and budget milestones. OR teams may use tools such as Gantt charts to create visual roadmaps that help them understand project timelines and dependencies. Digital data collection tools may be developed to simplify and to make the data collection process efficient. Training of field staff (if any are recruited for data collection) must be conducted to ensure that the field staff are well versed with the data collection procedures and are empowered to report on deviations in the data collection. It is always advised to do a pilot

project to pre-test and to identify any bottlenecks or challenges in implementing the study procedures.

Execution and data collection

During the project execution phase, the project team carries out the work required to complete the project. In this phase, project managers oversee data collection is carried out according to the protocol. Supervisory field visits must be carried out to identify and address any bottlenecks in data collection.

Monitoring and quality assurance

In many cases, this phase begins during the execution phase. Study investigators work together to monitor and compare project milestones and goals while making necessary adjustments to the schedule or budget. Mechanisms to ensure quality of data collection and data entry must be in place such as supervisory visits to observe on-field data collection, double data entry etc. If the project team is working to improve a process or output, this phase may include measurements of those outputs to help them know when they have reached success.

Analysis, report writing and dissemination

Once the data collection ends, the final phase of the project begins with data cleaning, data analysis and report writing. OR is incomplete if the data is not analysed, written up as a report and disseminated to all the stakeholders who need to know the results. This includes scientific/technical reports and a lay language summary of the study findings along with their implications for policy and practice.

Researchers have a diverse array of project management strategies, tools and software at their disposal. (1) The choice of which to use can be tailored to meet specific project requirements.

6.2   Are there any approvals or regulatory clearances that may be required for OR?

All OR must be undertaken only after the required administrative and ethical approvals have been obtained. If the OR involves secondary data analysis, then the approvals from the owners (public health programmes/projects) of the data will be required.

6.3   What are the budget considerations while undertaking an OR?

Researchers must identify the sources of the budget required to carry out the study. Depending upon the OR study, financial resources will need to be budgeted under the following budget heads.

- Human resources
- Workshops/ meetings (for training/review)
- Materials (e.g., diagnostics/drugs)
- Data collection (cost for data collection per participant)
- Field visits (for supervision)
- Reimbursements for participants (if they incur any expenses for participating in the research)
- Equipment and software
- Communication costs (e.g., telephone bills/internet connection)
- Costs for ethical approval
- Printing and office expenses
- Open access publication costs
- Dissemination costs (at conferences, to stakeholders)
- Institutional overheads
- Contingencies

The researchers must be pragmatic in preparing a budget proposal and obtain information on relevant unit costs. If the project involves multiple years, then budgets must be estimated taking into consideration the expected annual rate of inflation.

6.4   How should project management be presented in the OR proposal?

The OR proposal should include project management aspects, such as the names of the study investigators and their roles and responsibilities, the field investigator details, Gantt charts and the list of major and minor risks/challenges in implementing the research project and measures to mitigate or address them. Training, supervision and quality assurance of the data collection processes, if applicable, must also be included as a separate sub-section under methods in the OR proposal.

References

1.   Levin SP, Levin M. Managing ideas, people and projects: Organizational Tools and Strategies for Researchers. iScience. 2019; 20: 278–291. doi:10.1016/j. isci.2019.09.017.

7 Study variables and data collection formats

This chapter covers the types of study variables, their sources, selection, measurement and recording in OR studies. The chapter also gives an overview of measurement errors and steps that can be taken to minimise such errors. Finally, this chapter provides an outline for the presentation of study variables in an OR proposal.

7.1 What are study variables?

Variables are the pieces of information (data) that are collected in a research study in order to address the research question. The definition of a variable is 'an element, feature or factor that is liable to vary or change'. Its value may vary between data units in a population and may change in value over time.

Example:

An OR study aims to assess the various delays from onset of symptoms to the initiation of treatment among people with tuberculosis. These include delay in i) seeking care after onset of symptoms, ii) diagnosis of tuberculosis once a patient seeks care and iii) initiation of treatment once a diagnosis of tuberculosis is established. The study also aims to study if these delays are different based on patients' age, gender, history of tuberculosis or district of residence. The list of variables therefore would include at least:

- Name of district
- Age of patient
- Gender of patient
- History of tuberculosis in the past
- Time between onset of symptoms and visit to a health facility
- Time between visit to a health facility and diagnosis of tuberculosis
- Time between diagnosis of tuberculosis and initiation of treatment

7.2   What are the types of study variables?

There are multiple approaches to classifying study variables according to the ways they are studied, measured and presented.

- Qualitative versus quantitative variables

- Nominal, ordinal, interval, ratio variables

- Dependent versus independent variables

- Exposure versus outcome variables

The first classification above (qualitative versus quantitative variables) is discussed in further detail here as this classification is useful when one is designing an OR study to decide the format in which the data needs to be collected and the type of statistical analysis that would be required. It is important to note that qualitative variable is not related to "qualitative research design".

Figure 7.1 Classification of study variables
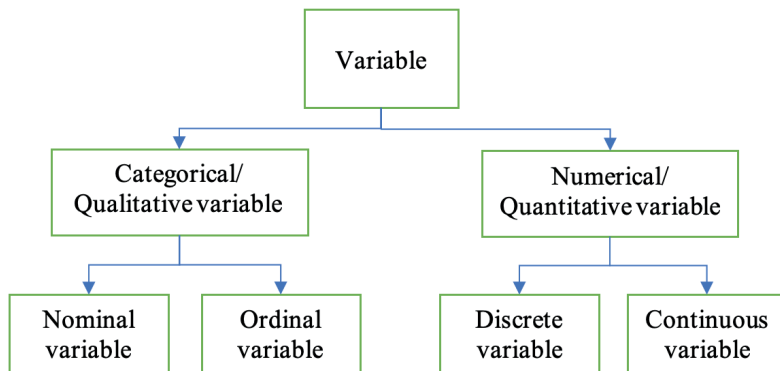
Qualitative versus quantitative variables

Data variables can be classified as either qualitative (categorical) or quantitative (numerical). Categorical variables are descriptive in nature whereas numerical variables are measurements where the numbers have some inherent meaning.

Categorical / Qualitative variables

- Nominal variables: These are variables that cannot be ordered or ranked. For example, sex is either male or female; facility type can be either a clinic or a community health centre; people with tuberculosis are categorised as new or retreatment.

- Ordinal variables: These variables are ordered with gradation over the category. For example, staging of HIV infection according to the WHO clinical stage 1, 2, 3 or 4; gradation of sputum smear microscopy is scanty, 1+, 2+ or 3+.

Numerical / Quantitative variables

- Discrete variables: The data can only take on certain whole numbers. The values of such variables do not overlap in any way. For example, the number of sputum samples submitted (1, 2, 3 etc.); the number of visits to the health facility (1, 2, 3, 4, 5, 6 etc.). A patient cannot have had 1.5 sputum samples submitted or 3.3 visits to the clinic.

- Continuous variables: The data may have a value anywhere along a continuum. For example, height may be measured in centimetres. The true height, if it could be measured, would be in centimetres with multiple decimal points and never finally arrive at the exact height. The point is illustrated similarly with age. The age could be said to be 52 years but is truly 52.546348…. And by the time this number is written, the age has already moved on several decimal points. For this reason, continuous variables are 'rounded' to a specified level.

7.3 How are study variables defined?

Although it might seem that the name of the variable is, in fact, its definition, this is not the case. Take, for example, the simple term 'individuals with tuberculosis'. What is its precise meaning in the context of the study? It might refer to any of the following patients:

- Those treated with a course of tuberculosis medication for the disease

- Those who have been bacteriologically confirmed with the disease

- Those who are sputum smear-positive

Each of these definitions can be found in one or other scientific publication and each is technically acceptable. However, they have quite different connotations. For example, if the study includes only bacteriologically confirmed patients, it will, by and large, exclude young children.

If the study includes only sputum smear-positive patients, it will exclude all those with extra-pulmonary disease and those with sputum smear-negative pulmonary tuberculosis. In places with a high burden of HIV infection, this definition may therefore exclude a large number of people with tuberculosis and HIV infection. If it includes all patients who were given any medication for treatment of the disease, it will exclude all those diagnosed with tuberculosis but never treated ('pre-treatment loss to follow-up') and include a certain number of patients with other serious conditions affecting the lung but who are incorrectly treated for tuberculosis (which is more frequent in patients living with HIV).

The precise definition of the terms used in scientific research is crucial to the quality of the research being undertaken. Each of the listed variables must be defined precisely to enable others to understand the terms used in the study and to replicate the study if they so desire.

Standardised definitions

Regarding tuberculosis, recognised standardised definitions are available and they are usually followed by national programmes. Examples include definitions of types of cases, drug resistance patterns, treatment outcomes, etc. Use of such standardised definitions allows comparison of findings across different programmatic settings. The source of these definitions should be appropriately cited in the study protocol.

Operational definitions

There could be instances where a well-established variable will need to be defined specifically for the research study. For example, a 'child' may be defined as a person in the age-group of 0-14 years by World Health Organization. (1) The definition of a 'child' according to national tuberculosis programmes may differ from country to country. For the purpose of a study evaluating HIV testing, a study may define a 'child' as <12 years (the age of medical consent).

There can also be instances where the researcher develops study specific variables which will need to be defined in the protocol. For example, if a study assesses whether tuberculosis treatment outcomes are 'favourable' or 'unfavourable, these need to be carefully defined. 'Cure' and 'treatment completion' are readily understood as 'favourable'. Unfavourable might include 'died', "treatment interrupted', 'loss to follow-up' and 'failed' but where does 'transfer out' or "not evaluated" belong? Unless specified, it would be unclear how this group has been dealt with.

In both the above instances, the researchers must clearly state the definitions that will be followed in their study. These are also referred to as 'operational definitions'.

Example: In the previous example of delays in treatment initiation, the 'delay between diagnosis and treatment initiation' may be defined in different ways.

- The 'time between diagnosis and treatment initiation' variable, often coined 'delay', may be defined based on a value considered appropriate to the services. If the mean delay for the study population is three days, delay in treatment initiation can be defined as any instance where the number of days between diagnosis and treatment initiation is more than three days.

- Alternatively, one may refer to the available literature which defines delayed treatment initiation. For example, treatment starting more than seven days after tuberculosis diagnosis is considered delayed.

7.4   What are the sources of data which may be available for OR studies?

Usually, data used in OR has already been captured in routine health records. Routine records for tuberculosis could include the Case Identification and Follow Up Register, Tuberculosis Clinic Card (a structured clinical record), Tuberculosis Register (at facility level), Laboratory request forms, Laboratory results sheets or laboratory records. These are also known as 'Secondary sources of data'. (2) With increasing digitisation of programme data, these sources may be available in paper-based formats, electronic formats or both.

At times data required to answer research questions in OR may not be readily available in routine records. The researcher may have to collect data first-hand for the purpose of research by employing different techniques, such as interviewing participants, conducting physical examinations, biochemical investigations, observing some processes in the field etc. These are also known as 'Primary sources of data'. (2)

For each variable, it is important to specify the data source that the variable was collected from. A missing sputum result in a clinical folder, for example, has a different connotation to a missing result in the laboratory database.

OR sometimes uses the same variable from two or more different sources for quality assurance purposes and to validate results, stressing the importance once more, of specifying the data source used. For example, the treatment outcome may be collected from the clinic card, paper-based tuberculosis register and the electronic tuberculosis register. When multiple data sources are used, it is important to describe the process of data validation, i.e., ensuring the data from different sources are reconciled and only the most accurate data is taken into considered.

7.5   How are study variables selected?

When thinking about the study data and variables, the researcher needs to answer the following questions:

- What is the research question or hypothesis?
- What exactly does the researcher want to analyse?
- What format must the data be in for analysis?

It is necessary to select only those variables that will help achieve the study objectives. While it may be tempting to include a large number of variables, especially when extracting data from available records, this practice causes more harm than good. It increases the work of data extraction, can be time consuming and prone to errors. When additional variables are collected without any well-defined plan or rationale, the subsequent data analysis also loses its focus. Most often, additional variables are ultimately not used in any meaningful analysis.

However, it is important to ensure that important variables required for answering the research question are not excluded. For this purpose, it is very useful to list variables according to study objectives at the time of designing the OR study. Existing literature, as well as experience and programmatic knowledge, provide a general idea as to which variables should be considered for inclusion in a study.

7.6   How are study variables measured?

Once the required study variables are listed, the researcher needs to decide how the variables will be measured as this is critical in determining the nature of analyses to be made.

- Record the highest level of detail possible. For example, collect the exact date of diagnosis and treatment initiation rather than days between diagnosis and treatment start. The duration between the two dates can be easily calculated at the time of analysis. Collect date of birth or age at treatment initiation rather than noting whether patients are in particular age groups. During analysis, the age can be categorised if required.

- Qualitative variables:
    - All categorical / qualitative variables have a range of 'categories' possible for each variable. The possible categories for tuberculosis treatment outcome, for example, include cured, loss to follow-up, died, failed, loss to follow-up, transferred out or not evaluated. From a data collection perspective however, some data may not be recorded, so 'not recorded' is also a possible category.

- o The range of categories must be carefully thought over, especially when dealing with variables which capture subjective information. For example, consider a study that is being conducted to rate patient satisfaction regarding laboratory services offered at a health facility. Patient satisfaction can be measured in multiple ways. i) Patient satisfaction may be captured as simply as 'Satisfied' or 'Not satisfied'; ii) The patient could be asked to choose an option that best describes their level of satisfaction: Extremely satisfied, Very satisfied, Somewhat satisfied, Somewhat dissatisfied, Very dissatisfied and Extremely dissatisfied; iii) The patient could be requested to rate satisfaction on a scale of 1 to 10 with 1 being Extremely dissatisfied and 10 being Extremely satisfied. All the three methods are valid but provide varying levels of granularity and require different modes of questioning.

- Numeric/quantitative: Numeric/quantitative data is further described by defining the range of possible values and the precision of measurement. For example, the acceptable range of weight in adults with tuberculosis can be set as 15.00 to 120.99 kg, which implies that the precision is 0.01 kg.

- Choice of tools for measurement: This is especially important when primary data collection is involved.

  - o Wherever possible, validated instruments must be used. For example, if an OR study aims to assess alcohol use disorders among patients at the time of tuberculosis treatment initiation, validated instruments, such as the Alcohol Use Disorders Identification Test (AUDIT) can be used instead of developing a new set of questions. This will improve the validity, acceptability and comparability of the findings.

  - o Whenever measurement of biological parameters (e.g., height, weight, waist circumference, blood pressure, heart rate, pulmonary function, blood glucose, kidney function tests, imaging, etc.) are involved, the method of measurement must be standardised and followed uniformly for all participants.

7.7   What are measurement errors and how can they be minimised?

All measurement / data collection has a certain level of error. Considering that OR often uses routinely collected data that is not originally recorded for research, errors in measurement are inevitable. This error can be either random or systematic as shown below.

Random errors in measurement	Systematic errors (bias) in measurement
Caused by factors that randomly affect measurement of the variable across the sample	Caused by factors that systematically affect measurement of the variable across the sample.
Can occur due to • Inherent biological variations within or between participants • Variations in the way researchers measure a variable • Fluctuations in measurement made by any instrument	Can occur due to • Selection bias (selection of a non-representative study population) • Information bias (incorrect determination of exposure or outcome) • Confounding (blurring of effect due to influence of an extraneous variable)
Unpredictable, therefore, difficult to control	Can be anticipated and addressed at various stages of the study
Can be reduced by increasing the sample size	Not affected by sample size
Statistics like p-value and confidence intervals are used to quantify random errors	Usually cannot be quantitatively measured or calculated

Random error

The effect of random error is to obscure a real difference between the groups being compared. If the error is random and not large, the likelihood of finding a true difference between the groups increases with the size of the population studied. (3)

Ways to reduce random errors in measurement include:

- Calculate the sample size and conduct research in an adequately sized study population so that the possibility of a result occurring by chance is reduced.

- Use instruments that have been validated and standardised.

- Double check all measurements for accuracy.

- Pilot test the measuring instruments/ questionnaires. For example, set up focus group and ask how easy or difficult the questions are to understand.

- Train the research personnel undertaking the measurements / data collection.

- Be systematic in taking the measurements / collecting data and design appropriate case report forms. Build in the provision of double-entry in crucial variables.

Systematic error or bias

Systematic errors result in finding a difference between groups when this difference does not actually exist. Several taxonomies exist for classification of biases in clinical research. A commonly used approach is to group all biases into three general categories: selection, information and confounding bias. (4)

Selection bias

Selection bias may occur if an inappropriate population is being studied, there is inadequate participation of the eligible population, the classification of the determinant changes over the study period or the study population consists only of the most accessible groups or volunteers. Always keep track of the exact number of persons who decline to participate.

Example: Assume that a study is designed to assess the pre-treatment loss to follow- up among people with tuberculosis, i.e., the number of people who are diagnosed with tuberculosis but not started on treatment. In this study, bias can be introduced by selecting only clinics in an urban area as these may have shorter turn-around-times (TAT) than semi-urban or rural clinics. If only clinics with on-site diagnostic services are included, the smear TAT may be very different in those clinics where persons being investigated submit sputum samples to be transported to the nearest laboratory.

The effects of participation in creating bias occur when participation in the study is selective in relation to the determinant and / or the outcome. This is why it is essential to report on the total eligible population and to determine what proportion of them actually participated in the study. If the proportion is very high (for example, over 80%), the possibility that bias may have occurred due to selective participation is much diminished.

To minimise selection bias, researchers should ensure that

- The population to be studied is appropriate to the question

- Every effort is made to ensure a high participation rate

- Comparisons are always presented of those who did and did not participate (for example, age, sex, residence).

Information bias

A change or variation in the way an outcome is defined or calculated can also lead to bias.

Example: In the pre-treatment loss to follow-up (PTLTFU) study above, one region may define PTLTFU rate as the % of patients with a confirmed smear result who fail to commence treatment within one week of the test being taken; another region may define it as the % of patients with a confirmed laboratory diagnosis who fail to commence treatment within one month of the test being taken; and a third region may define it as the % of patients with a confirmed laboratory diagnosis who fail to commence treatment within one month of the test result being available.

The PTLTFU rates are likely to be higher in the group that measures the outcome earlier as all the patients who commence from weeks 2-4 will be considered as PTLTFU in these clinics.

Example: One of the variables of interest in the PTLTFU study is the "Availability of a community health worker to do a follow-up visit or make a phone call for patients who have not commenced tuberculosis treatment". One researcher may answer this depending on whether or not a community health worker was available on the day of the visit by the field researcher. Another may answer it depending on whether or not a community health worker was available at any time in that facility. The first observer is more likely to report that community health workers were not available in the facility as she/he is basing their observation on a single day alone.

Ways to reduce information bias are listed below:

- During data collection, standardised protocols for data collection should be applied and data collection personnel should be trained to perform standardised data collection.

- During analysis, unrealistic values or outliers should be identified. Depending on the context, these observations may be dropped from analysis or retained with performance of sensitivity analyses. Even if any observations are dropped from analysis, they should never be deleted from the source file.

- If it is known that information bias could have occurred, this should be discussed upfront while the final scientific report/ research manuscript is prepared. Attempts should be made to assess the direction of bias.

Confounding

A 'confounder' is a factor that is associated with both the determinant and the outcome and consequently leads to a false association between determinant and outcome.

For a factor to act as a confounder, it must be independently associated with both the determinant and the outcome. In investigating the possibility of confounding, it is important first of all to test for an association with each of the determinants and the outcome. If the factor meets the criteria for confounding, an analysis of the association between determinant and outcome needs to be undertaken, stratifying for the presence or absence of the confounder. If the association between determinant and outcome persists after stratification for the potential confounder, the association can be accepted and the possibility of confounding rejected.

Example: Assume that a study is exploring the factors associated with death among those initiated on tuberculosis treatment. The study found that individuals with tuberculosis registered for treatment at tertiary care facilities had higher death rates compared to those in primary care facilities. In this study, the drug resistance pattern may be a confounding factor because:

- Drug-resistant forms of tuberculosis are known to be associated with increased mortality

- Patients with drug-resistant tuberculosis are more likely to be treated in the tertiary care facilities

- Drug resistance is not a consequence of being registered at a tertiary care facility

If information on drug resistance is not collected in this study, it may lead to false conclusions.

When selection bias or information bias exists in a study, the validity of the study is questionable. By contrast, when confounding is present, it can be addressed, provided that confounding is anticipated and the requisite information is gathered. Confounding can be controlled for before or after a study is done.

- Before the study

    o Restriction: If a confounder is known, then individuals with the known confounder are excluded from the study sample. However, this approach reduces the generalisability of the study and is also not feasible when there are multiple confounders.

o Random allocation: When the study has multiple comparison groups, allocation of participants to a group is done randomly in an attempt to even out unknown confounders. This approach is feasible only when the allocation to groups is under the investigators' control.

o Matching: Participants are recruited in such a way that the known confounders are distributed equally between study groups. The drawback of this approach is that i) the recruitment process can be cumbersome and ii) one cannot examine the effect of a matched variable on the outcome.

- At the end of the study, stratified analysis and adjusted analysis can be used to control for confounding provided data on potential confounders is collected.

7.8   How are case report forms developed?

Usually, the core data used in OR has already been collected in one or more of the sources listed in the previous section and exists in either a hard copy (paper) or electronic format. This data may be supplemented by information from primary data sources.

Whatever may be the source of data, a document will need to be designed to record all of the protocol – required information to be collected for the study. This document is known as the 'Case Report Form' or 'CRF'. The term CRF was first introduced in the context of clinical trials in which CRFs would capture information for each patient enrolled in the trial, hence the word 'Case'. (5) CRFs are crucial to OR as they can standardise data collection, helping to ensure that data is collected or extracted in a consistent way between different field researchers. CRFs can be paper based (data collected on paper forms and later entered in an electronic format for analysis) or electronic (data directly entered on to an electronic form which can then imported into statistical software for analysis).

The following guidelines are recommended when developing a CRF:

- Develop the CRF in a way that optimises both data collection and data entry.
- The questions in the CRF should follow a logical sequence. For example, data that is available at the start of a tuberculosis treatment card (e.g. demographic information such as age and sex) should be placed early in the CRF whilst data on tuberculosis treatment outcomes (available at the end of the card) should be placed towards the end of the CRF. Where data is collected from multiple data sources, the questions should be grouped according to the data source used to avoid field researchers having to move repeatedly between different data sources.

- The CRF should be simple and contain the minimum amount of information required. The data collected should be guided by the variables required for the study rather than the data available in the source document. The CRF should be easy to understand, easy to use and should not have any ambiguities.

- Ensure that the CRF has at least one variable which can serve as a 'Unique Identifier' which may be used to refer back to the source document or to link multiple sources of data. The tuberculosis registration number provided to each patient by the programme is a good example. When paper CRFs are being used, ensure that each page of the CRF contains this unique identifier so that pages can be linked together in case they get separated.

- Collect information exactly as it is recorded in the source document (secondary source) or as reported by respondents (primary source). Avoid the need for field researchers having to interpret information. For example, record the 'Number tuberculosis treatment doses taken' rather than expecting field researchers to answer the question 'Did patient receive the correct number of doses of tuberculosis medication?'

- Collect the highest level of detail possible. For example, collect the exact date of diagnosis and treatment initiation date rather than days between diagnosis and treatment start. Collect date of birth or age at treatment initiation rather than noting whether patients are in particular age groups. During analysis, the age can be categorised if required.

- Ensure that all possible responses are included in a question. The use of an option 'Other' should be kept to a minimum as this requires a substantial additional effort in post-coding once data collection has been completed. The range of response categories can often only be finalised once the CRF has been piloted.

- Make provisions to record if some information for a variable is not available or could not be collected. For example, include the response categories 'Not recorded', 'Not done', 'Refused to answer' and 'Not applicable' where appropriate.

- Avoid open ended questions as far as it is possible. For example: 'Chest x-ray report summary' or 'What type of training do staff receive on tuberculosis?' Post-coding of these responses is difficult and time consuming; consequently, these variables are often not analysed.

- Provide clear instructions, such as mandatory questions, skip logics (questions which are skipped based on responses to a previous question) and multiple responses, wherever required. For example, if information on key population groups is being collected, mention that a person could belong to more than one key population group so that the person collecting data remembers that multiple options can be selected.

- Provide adequate and appropriate space for recording answers. There are different ways to handle data in a CRF depending on the type of variable. With nominal, ordinal and discrete variables, check boxes may be used. Check boxes will ensure that the data collector is allowed to choose one of the possible answers, saves time and restricts errors which may creep in if the data collector is required to write down answers each time.

For date fields, boxes can be provided to represent the dd/mm/yyyy format.

The CRF should be piloted prior to its use in the study. This allows for the correction of simple errors, such as essential information that is missing or a poor sequence of data collection. Piloting of the CRF can only be undertaken after ethical approval is received. The pilot should be undertaken on a similar population to that used in the study but data is generally not included in the analysis. Both the investigators and the field researchers should be involved in piloting the CRF to ensure a common understanding of the questions and responses. The pilot data can be used to calculate 'dummy' outcomes as this will also help to ensure that all the required data is being collected.

7.9   How is data extraction planned if secondary electronic data sources are used?

In some situations, routine health information may already have been collated into an electronic format that is available for use. This substantially reduces the effort required to undertake the research. However, there are a few important considerations:

- At the time of developing the protocol, the researcher should be familiar with the structure of the electronic database. It is best if the data is exported in a spreadsheet format (basic formats include .xls or .csv) to facilitate import into the statistical analysis software. There have been instances where the existing databases do not have the provision for a spreadsheet export or export in formats (like pdf) which cannot be used for analysis. Then the only option is to enter data into a spreadsheet format and this needs to be planned in advance.

- Even though the data may be readily available in a spreadsheet format for analysis, it is a good practice to list out the specific variables required for answering the research question. Focus on the availability, completeness and quality of these variables.

- The accuracy of information in the database should be assessed, especially if the database has been developed by manually transcribing information from paper records. This can be done by taking a sample - about 10% of records – and reviewing these against the original source documents (e.g. clinical records) to determine the rate of transcription errors. If the quality of data is poor for key determinant and outcome variables, it may not be possible to use the electronic records.

7.10   How are study variables presented in the OR proposal?

To summarise, the following aspects related to study variables should be described in an OR protocol:

- List of variables and sources from which data will be collected (according to study objectives)

- Definitions for variables, wherever applicable

- Data collection instruments: The CRF should ideally be included as an Appendix to the protocol

- Plan for data collection in the field.

References

1. Global Tuberculosis Report 2022 [Internet]. [accessed 24 August 2023]. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022.

2. Common Data Types in Public Health Research | NIH Library [Internet]. [accessed 24 August 2023]. Available from: https://www.nihlibrary.nih.gov/resources/subject- guides/health-data-resources/common-data-types-public-health-research.

3. Myer L, Morroni C, Link BG. Impact of measurement error in the study of sexually transmitted infections. Sexually Transmitted Infections. 2004; 80(4):318– 21.

4. Grimes DA, Schulz KF. Bias and causal associations in observational research. The Lancet. 2002; 359(9302):248–52.

5. Bellary S, Krishnankutty B, Latha MS. Basics of case report form designing in clinical research. Perspect Clin Res. 2014; 5(4):159–66.

8　　Data capture

This chapter deals with the modalities for data capture and the types of databases that can be employed in OR. It also covers the issues to be taken into consideration for quality assured data capture, data confidentiality and long-term data storage. Finally, this chapter provides an outline for the presentation of data capture in an OR proposal.

8.1　What are the modalities available for data capture?

Data capture is the process of collecting or extracting information from any type of document and transforming it into a machine-readable digital format. In simpler terms, it is the process of collecting information and then changing it into a form that can be read and used by a computer. In the context of OR, data capture could mean:

- Transfer of data already available in paper-based registers or records (secondary sources of data) to an electronic CRF/database designed for the study.

- Extraction of selected data points from an existing electronic database (secondary sources of data) into an electronic CRF/database designed for the study.

- Transfer of data collected on paper-based CRFs during the research study to an electronic CRF/database.

- Real time entry of data collected during the research study onto an electronic CRF/database.

There are various electronic platforms available for data capture. Those commonly used in public health research are:

- Form building and data entry
    - o Mobile phone-based or Desktop based applications: Epicollect, ODK Collect, RedCap, Epi Info, Google forms (1-5)
    - o Desktop based software packages: EpiData Classic, EpiData Manager, CS Pro, MS Access (6–8)
- Data entry: MS Excel, SPSS, Stata. However, these are not developed for database management and their use for data capture is discouraged.

8.2 What are the different forms of databases that can be developed in OR?

A database is an organised electronic collection of data. Conceptually, data in a database is organised into files called tables. (9) A table contains rows (or records) and columns (or variables), where each field for a given row is a data element. Broadly there are two types of databases:

- **Flat file database** contains a single table of data. This is adequate when the database is fairly small and when a one-to-one relationship of data is required for single line data. It is suitable for most simple OR studies and for questionnaires. However, it is not suitable for large complex datasets or where matching is required across different data sources.

- **Relational database** contains multiple tables of data that relate to each other through special key fields. Relational databases are far more flexible (though harder to design and maintain). They are recommended when more complex data is used and a one-to-many relationship is required. Most electronic data capture modalities used in public health research support development of relational databases. (10)

Example: A study in which patients diagnosed with pulmonary tuberculosis are enrolled at the time of treatment initiation (baseline) and followed up at six monthly intervals for two years after treatment completion to assess long term impact of tuberculosis on pulmonary function. For each patient who is enrolled, there is a baseline data collection CRF which records socioeconomic and clinical characteristics and results of the baseline pulmonary function tests. Subsequently, at each follow-up pulmonary function tests are repeated. Assume that data is updated on an electronic CRF on a real time basis. This study will require a relational database with two tables: one for capturing data from the baseline CRF where each row stands for baseline data of a patient and the other for capturing follow-up data where each row stands for pulmonary function test results recorded at each follow-up. At the time of analysis, the two tables will be merged using a unique identifier (such as patient enrolment ID) so that each patient's baseline and follow-up data are available in a single file for analysis.

8.3   How to ensure quality assured data capture?

It is important to acknowledge that it is human to make errors during data capture and researchers need to take steps to minimise errors as much as possible. The following are good practices which help ensure quality assured data capture:

Data dictionary: A data dictionary is essential for data documentation in all research studies, irrespective of whether these collect primary data, use data from existing clinical records or from an existing electronic data source. The development of a data dictionary forces the researcher to think logically about the structure and the format of data to be collected. The data dictionary should contain at least the following information for each data variable to be collected:

- Variable name

- Variable description

- Type of variable

- Length

- Possible answers: value / format / range (permitted values)

- Logic checks (e.g., root versus nested question: cannot have number of pregnancies completed if sex was recorded as male)

- Missing values (e.g. -99=Unknown) – make sure that the symbol used for the unknown value is not a value that can occur in the real data for that or any other variable.

Numeric coding for categorical variables: The categories may be recorded either as numbers or as text. It is standard practice to collect data from the source documents as text and to transform these into numbers for data capture. The use of codes/numbers is preferable as it is less prone to data entry error than typing the text would be. The close proximity of the numeric keys on a personal computer also facilitates rapid data entry. This not only provides more efficient handling of data but also sets up the information in a way that can be easily managed for statistical analysis. For the 'tuberculosis treatment outcome' variable for example, the different categories would be coded as follows: 1 – cured, 2 - treatment completed, 3 – died, 4 – failed, 5 - lost to follow-up, 6 - transferred out, 7 - not evaluated, 99 - not recorded.

Data quality checks built into the data capture platform: When developing a database, the time invested in system development can pay dividends as a well-designed database reduces errors during analysis. Most of the currently available software applications which are designed for data capture allow incorporation of data quality checks, such as

limiting the range of values for numerical variables and the possible answers in categorical variables, skip logics and compatibility checks. These are very useful for reducing errors at the stage of data capture and should be well thought through when developing the data dictionary and then applied while developing the data capture tools.

Standard Operating Procedures (SOPs): A data collection SOP should be developed that sets out all of the pertinent issues from selection of records to be reviewed, to collection of data elements, to handling of missing records or data, to checking the CRF for completeness before leaving the facility and other quality assurance checks.

Double or dual data entry: Dual data entry is a process by which two people capture the same data separately on identical databases. Each person has their own copy of the database and comparison is done: all discrepancies are checked with the original source. The rationale for this is that it is only human to make errors (often at a rate of about 10%) during the data capture process. However, when two people capture the data and then the two data sets are compared and corrected by verifying against the original source document, the error rate drops dramatically.

Timely entry and quality checks: It is important to ensure that there is no lag or just a minimal lag between data collection or extraction and entry into the data capture platform. This is especially important when data from paper-based sources is captured on an electronic platform, as there is a risk of loss of data from the paper-based sources during the lag time. A systematic process of periodic data quality checks should be set up, so that data can be reviewed on an ongoing basis and errors identified and corrected whilst the study is ongoing. It is advisable to periodically validate a pre-specified proportion (e.g., 10%) of entries made on the electronic platform by comparing it with the original data sources.

8.4   What are other aspects to be considered in data management for research?

In the previous chapters, we have discussed the process of selecting study variables, their measurement and recording of study data. In addition, data management also includes:

- Planning for statistical analysis: How will the data be analysed and presented?

- Storage, back-up and security: How and where and for how long will the data be stored and how will it be secured?

- Provisions for protection/privacy: What privacy and confidentiality issues may arise and how will they be addressed?

- Policies for re-use: How can other researchers access and use data from the study? It is important that a process for ethics review and permissions to re-use data are put in place if such re-use is expected.

- Sharing: How and with whom will the results be shared?

- Archiving and providing access: Are there any plans for preserving the data and providing long-term access? To ensure transparent reporting, researchers are increasingly being encouraged or even mandated (by some journals) to make research data available to the scientific community at the time of publication. This can be done by uploading the data to a repository, such as Zenodo, Figshare, Science Data Bank etc. Upon uploading data to the repository, it is assigned a Digital Object Identified (DOI) making it independently citable. (11)

- Roles and responsibilities: Who will be responsible for aspects of data management throughout the project and what resources are required for implementation?

A data management plan, or DMP, is a formal document that outlines how data will be handled during and after a research project. Some funding agencies require a DMP as part of their application processes. Even if it is not a requirement from the funder, documenting a plan for managing research data is the best practice and will help the collected data comply with good clinical practice (GCP) requirements and ethical standards.

Data management starts right at the beginning - during proposal development. The proposal needs to address data requirements and data management. This needs to be carefully thought through as it has budget implications, including for the following:

- Equipment and consumables (e.g., computers, printers, cartridges, toners)

- Software or computer programmes

- Data collection tools (either paper-based or electronic)

- Stationery (e.g., paper, envelopes, labels, barcodes, black pens, clipboards, files)

- Staff (data manager, database developer, data capturers)

- Data storage and back-ups (electronic and hard copy).

8.5 What steps should be taken to ensure that confidentiality of collected data is maintained?

In handling any information from records, strict procedures are required to ensure the confidentiality of the information that is collected and analysed. An essential and integral part of good clinical practice and ethical principles is to maintain confidentiality and not to use the names of individuals when collecting and analysing data. The exact manner in which data will be accessed and steps taken to ensure confidentiality will have to be laid out in the protocol, explained to the ethics committee and only when the approval has been granted, can the study go ahead.

Sometimes the only way to access data is to use names. In some instances, personal identifiers (names, dates of birth, address, etc.) may be required to perform record linkage. There may be instances where the study entails follow-up of patients and identifiers may be required for tracing the patient.

The principle is to preferably use unique study numbers and not to have the name and study results in the same document, electronic spreadsheet or database. The best practice recommendation for accessing data without having the name of a client on the same form as the results to be collected is to compile two lists:

- A list with subject name, surname and unique study code. This will be used only during the study data collection period for linking different sources of data or for contacting patients if mandated by study protocol. Processes to ensure that this list of personal identifiers is destroyed after linkage is complete should be described.

- A different list with the unique study code and results. This list without any personal identifiers will be used for the purpose of analysis.

8.6 What are the considerations for data storage during and after completion of research?

The following are the considerations for data storage at the different stages of OR.

Data storage during the study period: There are several storage options such as paper-based files, desktop computers and laptops, networked drives, external hard drives, optical storage and cloud storage. Data must be stored securely in a safe or locked be protected with passwords which themselves should be protected as carefully as study data. Secure methods of file transfer should be used whenever confidential data is shared with researchers.

Data back-ups: Regular back-ups and appropriate storage of the back-ups are essential for all electronic databases using the schedule suggested below:

- Daily – keep the most current back-up off-site

- Weekly back-ups (keep for at least a month)

- Monthly back-ups (keep for six months)

- Quarterly back-ups (keep for a year)

- Six-monthly backups (keep for five years).

Locked database: After data have been captured, validated and all queries resolved, the database should be locked and a copy of the locked database should be stored safely. The locked database should never contain patient names and should be stored safely (including at least two back-ups stored in different locations). The original locked database should never be used for analysis and a copy is made to work on; if the original database is used and a mistake is made or the database becomes corrupt, it may be impossible to analyse the data.

Long term data archival: A plan for data storage is essential as all data must be stored for a minimum of five years (the period may vary depending upon country-specific ethical guidelines). Data can be stored either in electronic format or in hard copies or preferably, in both. All paper documents must be kept for a minimum of five years. Long term storage requires a lockable facility which is preferably safe from natural disasters, such as floods, fire and other destructive elements, e.g., rats and moths. As a further precautionary mechanism against water damage from burst water pipes or floods, never store data directly on the floor, always store it on shelves.

Data and documents should be stored in a logical format for later retrieval e.g., by study site or by date or by unique identifier. The consent forms and the linking lists which contain names should always be stored in a separate locked filing cabinet with restricted access.

8.7 How should data capture be presented in the OR proposal?

To summarise, the following aspects related to data capture should be described in an OR protocol:

- Procedures for data entry: Software or application for data capture, timing of data capture (real time or not)

- Steps taken to ensure confidentiality and safety of the electronic database

- Any data quality assurance mechanisms that will be implemented (such as double data entry, random data validation or data verification with source documents).

References

1. Epi InfoTM | CDC [Internet]. 2022 [accessed 24 August 2023]. Available from: https://www.cdc.gov/epiinfo/index.html

2. Google Forms: Online Form Creator | Google Workspace [Internet]. [accessed 24 August 2023]. Available from: https://www.facebook.com/GoogleDocs/

3. ODK Collect - ODK Docs [Internet]. [accessed 24 August 2023]. Available from: https://docs.getodk.org/collect-intro/

4. Software – REDCap [Internet]. [accessed 24 August 2023]. Available from: https://projectredcap.org/software/

5. Free and easy-to-use mobile data-gathering platform. [Internet]. [accessed 24 August 2023]. Available from: https://five.epicollect.net/

6. Buy Microsoft Access, Application & Database Software for PC [Internet]. [accessed 24 August 2023]. Available from: https://www.microsoft.com/en-in/microsoft-365/ access

7. CSPro Software [Internet]. [accessed 24 August 2023]. Available from: https://www.census.gov/data/software/cspro.html

8. EpiData Software - http://www.epidata.dk [Internet]. [accessed 24 August 2023]. Available from: https://www.epidata.dk/

9. Flat file and relational databases [Internet]. [accessed 24 August 2023]. Available from: https://kb.iu.edu/d/ahrp

10. Relational Database vs Flat File (Differences & Similarities) - DatabaseTown [Internet]. 2023 [accessed 24 August 2023]. Available from: https://databasetown.com/ relational-database-vs-flat-file-differences-similarities/

11. Data Repository Guidance | Scientific Data [Internet]. [accessed 8 August 2023]. Available from: https://www.nature.com/sdata/policies/repositories#genera

9 Data analysis

This chapter discusses the approach to data analysis in OR. It provides an overview of the summary and inferential statistics measures used in OR based on the study design. Finally, this chapter provides an outline for presenting a data analysis plan in an OR proposal.

9.1 What are the key elements of the data analysis plan in an OR study?

The key to a data analysis plan is to ensure that the analysis can answer the research questions or address the objectives of the OR study. While planning the data analysis, it is imperative to ensure that the data variables required for answering the research question are captured appropriately. (1)

Example: The objective of an OR study is to describe the programmatic tuberculosis treatment outcomes of people with drug-sensitive tuberculosis initiated on treatment in 2022 in a city X. These outcomes are cured, treatment completed, death, lost to follow-up, failure and not evaluated. If the data collectors captured treatment outcomes as either 'successful' (cured and treatment completed) or 'unsuccessful' (death, lost to follow-up, failure and not evaluated), it is impossible to address the objectives. This is because the data collectors have classified the treatment outcomes as 'successful' and 'unsuccessful' during data extraction. To describe the programmatic tuberculosis treatment outcomes, the outcomes should have been captured as recorded in the tuberculosis treatment card, namely cured, treatment completed, death, lost to follow-up, failure and not evaluated.

Thus, before deducing the data analysis plan, it is essential to map data variables relevant to each objective or research question and understand how the variables are captured (type of variable and level of disaggregation). The choice of summary and inferential statistics depend on the type of each variable (categorical, ordinal, discrete or continuous) that we consider for analysis. (2)

The summary statistics help to describe or summarise the findings of individuals included in the study (Figure 9.1). Sometimes researchers will adopt a random sampling strategy to include only a subset of the study population. Using the study sample, they extrapolate the study findings to the whole of the study population using inferential statistics. So, they always deduce summary statistics to describe the study participants first and later carry out inferential statistics if the conditions for deriving inferential statistics are met.

Figure 9.1 Summary and inferential statistics
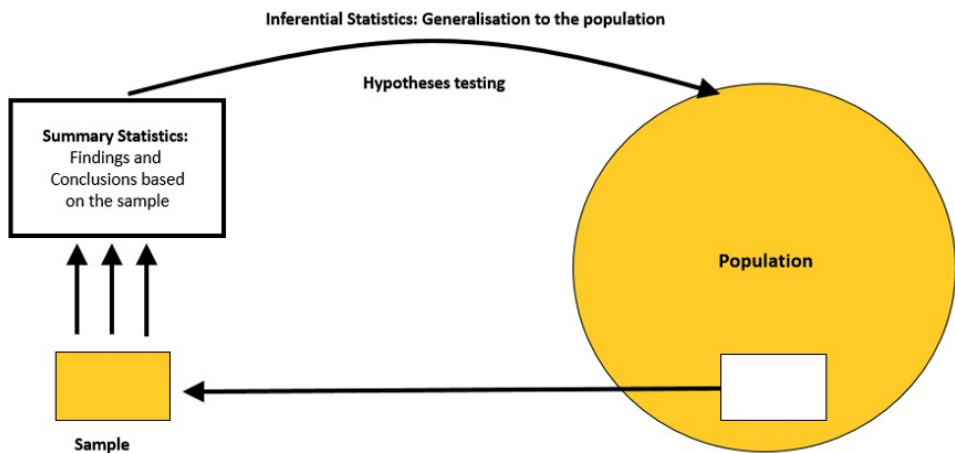
Another key data analysis consideration is the study design adopted for the OR. (3) The approach to data analysis in a descriptive study is different from that in an analytical study (including experimental study). In this chapter, we have provided an approach to data analysis based on the study design adopted for the OR. This will enable the reader to choose appropriate statistical measures and draft the data analysis plan based on the study design.

9.2 What are the key elements to data analysis in an OR study with a descriptive design?

There are certain key elements that need to be considered if the OR is descriptive in nature (example, one study group) without any hypothesis testing. (4) The researchers have to answer questions presented below to choose appropriate summary and inferential statistics.

9.2.1 What summary statistics measures can be used?

The researchers have to look into each of the variables and decide whether the variable is categorical or numerical and, if the latter, are they discrete or continuous. In case of a continuous variable, the researchers need to determine whether it is normally distributed or not. At the stage of the protocol development, it is probably unlikely that the researchers will be able to decide on the distribution, unless they are sure that the selected continuous variable will not follow a normal distribution due to extreme variation or small sample size. Thus, the researchers may have to wait till the completion of the study to decide on the distribution.

Frequencies and percentages are used for summarising categorical variables. In case of continuous variables, mean and standard deviation is used if there is a normal distribution or median and interquartile range is used if the distribution is not normal. In case of discrete variables, median and interquartile range can be used (Table 9.1).

Table 9.1 Type of variables and the appropriate summary statistics

Type of variable	Summary statistics
Continuous, normal distribution	Mean with Standard Deviation
Continuous, not normal distribution	Median with Interquartile Range
Discrete	Median with Interquartile Range
Categorical	Frequency with Percentage: Proportion, Rate and Ratio

Example: To understand the above questions better, let us discuss an OR study conducted to assess the programmatic tuberculosis treatment outcomes among migrant pulmonary TB patients initiated on first-line tuberculosis treatment during the year 2022. Assume that the researchers have collected the variables, such as age in completed years, gender (male/female), type of case (new/previously treated), type of diagnosis (bacteriologically confirmed/clinically diagnosed), number of household contacts and programmatic treatment outcomes (cured, treatment completed, death, lost to follow-up, failure and not evaluated).

All the above variables except age in completed years and the number of household contacts are categorical variables and can be summarised using frequency and percentage (proportion). As the number of household contacts is a discrete variable, median and interquartile range must be used. For age in completed years, we need to check whether it is normally distributed or not. We can use mean and standard deviation if normally distributed, if not, then median and interquartile range.

9.2.1.1 What are mean and standard deviation? When to use them?

Mean is a measure of central tendency and   summarises continuous data into a single value. (2) The single summary value is usually the central value of the data set. However, it depends on the distribution of the data. The mean of a sample is calculated by adding up all of the observations and dividing by the number of observations. Suppose we draw a sample of five women and measure their weights. They weigh 50kg, 50 kg, 65 kg, 70 kg and 75 kg.

$$\text{Mean weight} = (50 + 50 + 65 + 70 + 75)/5 = 310/5 = 62 \text{ kg}$$

The advantage of using mean is that it represents observations from all the study participants and it is easy to interpret. However, mean is affected by outlier values. When the dataset has a large value which is an outlier, it will pull the mean towards the higher value resulting in skewed results. For instance, in the above example, if the weight of the fifth participant is 200 kg instead of 75, the calculated mean will be 87 kg instead of 62 kg. It is clear from this example that if there is a large value (one or a few values as outliers), the mean will be skewed towards the large value and other values will be minimally represented. Thus, mean can be used as a measure of central tendency only when the normal distribution exits without any outliers.

Standard deviation (SD) is one of the commonly used measures of dispersion for quantitative variables. (2) Standard deviation is the positive square root of the mean of squared deviations from the mean. Standard deviation is a measure of dispersion used consistently with the mean, which is a measure of central tendency. Standard deviation indicates the spread of data from the mean. For example, one standard deviation indicates that 68% of data values are spread on either side of the mean.

Similarly, two standard deviations indicate that 95% of data values are spread on either side of the mean. This will be discussed further in the section (9.2.1.3) on normal distribution.

Example: If the mean and standard deviation of weight of the study participants are reported in scientific journals as 67 (17) kg or 67 ± 17 kg, it means that 68% of the weights of the participants are between 50 (67-17) and 84 (67+17) kg. Similarly, 95% of the study participants have the weight between 33 (67-34) and 101 (67+34) kg (Figure 9.2).

Figure 9.2 Relationship between mean and standard deviation
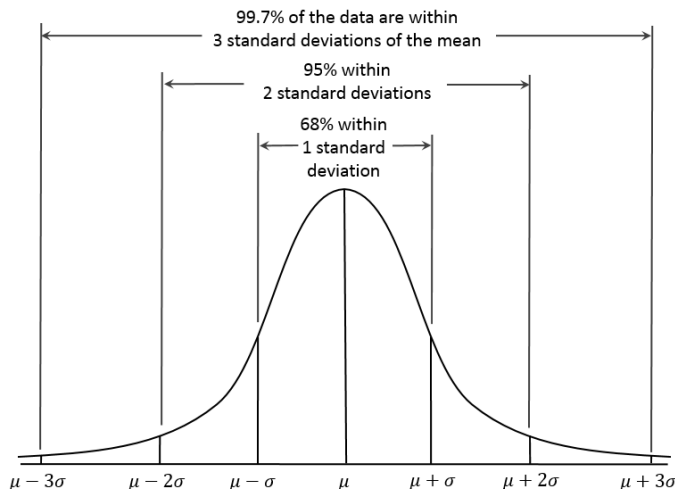
The mean and standard deviation are used to summarise the continuous variable (not discrete variables) only when it follows a normal distribution.

9.2.1.2 What is median and interquartile range? When to use it?

Median is another measure of central tendency which indicates the central value of the given data set. (2) The median is the point in the distribution above and below which 50% of the observations lie. In other words, if the observations are listed in order from highest to lowest (or lowest to highest), the observation that lies in the middle is the median. Let us use the same example of weight of the five women. They weigh 50kg, 50 kg, 65 kg, 70 kg and 75 kg.

Median weight = 65 kg

The advantage of the median is that it is not affected by the extreme/outlier values, including skewed data and can be derived even when the data does not follow a normal distribution. For instance, in the above example, if the weight of the fifth person is 200 kg instead of 75, the calculated median will remain 65 kg.

The median is always presented with the interquartile range (IQR) as the measure of dispersion. As the name implies, quartiles are values that divide the whole data into four equal fragments. Hence, there will be three quartile values, i.e., 25%, 50% and 75% (positioned at 25th, 50th and 75th percentiles of the data). (2)

Interquartile range and median values divide the data into four equal quarters. The first (Q1) quartile value indicates that a quarter or 25% of values are below this value. Similarly, third (Q3) quartile value indicates that 75% of the values in the data are below this value. The advantage of using interquartile range is that it is not affected by extreme values and can be used in data that is not normally distributed or has a small sample size. It provides better representativeness and dispersion of data. Thus, the median and interquartile range are used to summarise discrete variables and also continuous variables that do not follow a normal distribution.

9.2.1.3 How to check for normal distribution?

It is important to check for normal distribution for the continuous variables as the choice of summary statistics depends on whether or not there is a normal distribution. (5)

When the histogram is plotted for a continuous variable, if the data is distributed equally on either side of the mean value (midline), the data can be said to be normally distributed. Also, when the observations are equally distributed on either side of the mean value, then the mean will be almost the same as the median (Figure 9.3).

Figure 9.3 Structure of the histogram and normal distribution curve
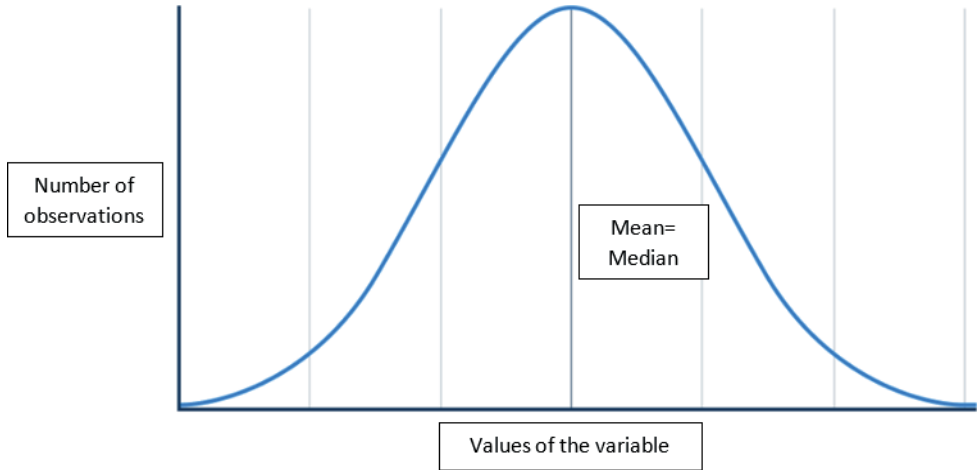
A normal distribution can also be checked using statistical tests, such as Kolmogorov-Smirnov test and Shapiro-Wilk test. These tests require either software for statistical analysis or manual mathematical calculation to ascertain the normality of the data.

Another way to determine normal distribution is by this rule of thumb: the standard deviation should be less than half of the mean to have data with normal distribution. For example, if the mean is 30, then the standard deviation should be less than 15. This rule of thumb is sufficient to determine the normal distribution in an OR study.

9.2.1.4 How to summarise the categorical and ordinal variables?

Categorical and ordinal variables are summarised using frequency and percentages. (2) It is not appropriate to summarise them using mean (standard deviation) or median (interquartile range). In a study assessing the programmatic tuberculosis treatment outcomes, the "tuberculosis treatment outcome" is a categorical variable with cured, treatment completed, lost to follow-up, died, failure and not evaluated as the categories. We can report the number (frequency) of patients who are cured as one of the treatment outcomes and the percentage of this in relation to all people with tuberculosis included in the study.

Although frequency and percentages are the standard measures used for summarising the categorical or ordinal variables, the percentages can be in the form of **ratios**, **proportions** and **rates**.

Ratio

A ratio is the division of two different numbers (frequency measures) or magnitudes or quantities. The two values (numerator and denominator) need not be related to each other. The numerator is not part of the denominator. Ratios generally do not have units of measurement attached to them when reported.

Example: Gender ratio = (Number of women) /(Number of men)×1,000

The ratios can be reported as 987 women per 1,000 men.

Proportion

A proportion is the ratio of the number of subjects with a given characteristic (numerator) to the total number of subjects in the group (the denominator). The numerator is always the subset of the denominator. Proportion provides the summary of the occurrence of events among the study participants. Proportions can be expressed as percentages or fractions.

Proportion = (Number of individuals with the event of interest in the study group)/ (Total number of study participants) x100

Example: In an OR study assessing the programmatic tuberculosis treatment outcomes, 1,000 people had extra-pulmonary tuberculosis among the 5,000 people with tuberculosis included in the study.

Proportion = (Number of individuals with extra-pulmonary tuberculosis)/ (Total number of people with tuberculosis included in the study) x100

            = (1,000/5,000) x100

The proportion of people with extra-pulmonary tuberculosis among all the people with tuberculosis is 20%. This is the prevalence of extra-pulmonary tuberculosis among the people with tuberculosis in the study.

Rate

Rate is a measure of the occurrence of events in a specified population over a specified period of time. Rate is similar to proportions with the numerator being part of the denominator but with a time component included. Unlike ratios, rates have units attached to them. Thus, rates can be used for the occurrence of disease in a population in a specified time or occurrence of adverse effects in a group of people taking specific medication, etc.

Rate = (Number of individuals with the events in a specified time)/ (Total number of individuals followed during the specified time) x1,000

Example: In a study assessing the burden of adverse drug events among people with tuberculosis initiated on first-line treatment, 50 developed adverse events among 5,000 individuals followed-up for a period of six months.

Rate = (Number of individuals with the adverse events in six months)/ (Total number of TB patients followed-up for six months) x1,000

Rate of adverse events over six-months= 10 adverse events per 1,000 population followed for six months. As these are newly occurring events, the rate is the incidence rate of adverse events over six months of follow-up.

The rate can also be expressed in terms of person-months or person-years of follow-up. As 5,000 patients are followed-up for a period of six months, they contribute 30,000 person-months (5,000 individuals × 6 months) or 2,500 person-years (5,000 individuals × 0.5 years). The rate of adverse events can also be mentioned as 1.7 adverse events per 1,000 person-months of tuberculosis treatment (50 × 1,000/30,000 person-months) or 20 adverse events per 1,000 per-years of tuberculosis treatment (50 × 1,000/2,500 person-months).

9.2.2 What inferential statistics can be used in a descriptive study?

Sometimes a random sampling strategy is adopted to include only a subset from the study population. Using the study sample, we try to extrapolate the study findings to the whole of the study population using inferential statistics, such as 95% confidence intervals (CI).

This issue of inferential statistics arises only when a random sample is taken from the study population. Ideally, in OR studies where the whole of the study population is included, there is no need for calculating the inferential statistics. However, some researchers prefer calculating inferential statistics, such as 95% confidence intervals even when the whole study population is included to accommodate for time sampling which happens during inclusion of study participants.

Example: While assessing programmatic tuberculosis treatment outcomes of migrants initiated on treatment in the year 2022, we are sampling migrants with tuberculosis in terms of their tuberculosis treatment initiation in the year 2022. Thus, the migrants with tuberculosis initiated on treatment in 2022 would be the subset of all migrants with tuberculosis initiated on treatment anytime. Thus, it is better to calculate the inferential statistics for the key outcome variables.

If the plan is to calculate the inferential statistics, it is important to ensure that the sample size is adequate to derive a precise estimate of 95% confidence intervals for the study population.

This highlights the importance of calculating the minimum sample size for the study and ensuring the calculated sample size for the study is met.

Example: In the above-mentioned OR study conducted to assess the programmatic tuberculosis treatment outcomes among migrants with pulmonary tuberculosis initiated on first-line tuberculosis treatment during the year 2022. Assuming that the study was conducted in a randomly derived sample of migrants with pulmonary tuberculosis and the minimum sample size has been met, let us plan for the appropriate inferential statistics. Though we might have collected several demographic and clinical variables, we will only be interested in calculating the inferential statistics for the programmatic tuberculosis treatment outcomes which is the key outcome variable of interest in the study. We will present 95% confidence intervals with the summary statistics of frequency and percentage for programmatic treatment outcome categories, i.e., cured, treatment completed, death, lost to follow-up, failure and not evaluated. The frequency and percentage will provide the summary of the sample in the study whereas the 95% confidence intervals will provide an estimate of the study population.

9.2.2.1 What is 95% CI?

A confidence interval (CI) is a range of values within which the "true" population proportion is believed to be found with a given level of confidence. (6) The rationale for calculating confidence intervals is the uncertainty which is always associated with using samples to make inferences on the populations from which these samples originate. A 95% confidence interval means that we can be 95% confident that the true population value lies within its limits.

Example: In a study of programmatic tuberculosis treatment outcomes among migrants in Site X, 100 were cured among 500 included in the study. The proportion with the outcome 'cured' was 20% (100/500). The calculated 95% confidence interval was 16.7% to 23.7%.

In this example, the implication is that we can be 95% confident that the cure rate among the migrant population with tuberculosis would lie anywhere between 16.7% and 23.7%. Remember, however, that there is still a 5% risk that true population proportion lies outside this interval.

Similarly, the 95% confidence interval can be even calculated for the mean and median. In case the outcome of interest is a continuous or a discrete variable, the 95% confidence interval can be calculated for the mean or median based on the distribution. For example, the mean (standard deviation) weight gain among 500 migrants with tuberculosis at the end of their tuberculosis treatment is 3.0 kg. The 95% confidence interval would be 2.9 to 3.1 kg. The implication is that we can be 95% confident that the weight gain among the migrant population with tuberculosis at the end of tuberculosis treatment would lie anywhere between 2.9 and 3.1 kg.

9.2.3 How to develop a data analysis plan for descriptive study?

In the OR protocol, the data analysis plan has to be detailed in the methods section. It is important to highlight the following items:

1. The software that will be used for data entry and analysis, including the version of the software.

2. The summary statistics that will be used for summarising each of the variables included in the study.

3. Inferential statistics that will be used for extrapolating the findings to the study population, if a random sample is used and the sample size is adequate.

Example: For an OR study conducted to assess the programmatic tuberculosis treatment outcomes among migrants with pulmonary tuberculosis initiated on first-line tuberculosis treatment in 2022, the data analysis plan is provided below.

"*Data will be double entered and validated using EpiData entry version 3.1 (EpiData Association, Odense, Denmark). The analysis will be conducted using Stata 11.0 (StataCorp LP, College Station, TX, USA). The categorical variables, such as gender, type of case and type of diagnosis will be summarised using frequency and proportions. The age in completed years will be summarised using mean with standard deviation or median with interquartile range based on the normal distribution of data. The number of household contacts will be summarised using median with interquartile range. The frequency and proportions with 95% confidence interval (inferential statistics) will be calculated for the programmatic tuberculosis treatment outcomes.*"

9.3 What are the key elements to data analysis in an OR study with an analytical design?

The focus of the analytical studies (cross-sectional analytical, case-control and cohort studies including experimental designs) is to assess the association or relationship between two variables.

In addition to the elements considered for analysing the descriptive studies, there are three additional elements that need to be considered while deducing an analysis plan for OR studies with an analytical design. They are:

1. Independent (exposure) and dependent (outcome) variables.

2. Hypothesis testing for association: tests of significance, such as t test, chi square test, etc. (2)

3. Measures of association: mean difference, relative risk, prevalence ratios and Odds Ratios.

In this entire section, we will use an example of the analytical study to assess whether there is any association between migrant status and unsuccessful treatment outcomes among people with pulmonary tuberculosis initiated on tuberculosis treatment during 2022 in the city X. Here the interest is to see whether migrant status affects the unsuccessful treatment outcomes and if it does, how big is the effect. So, using simple random sampling, we include 500 migrants with tuberculosis and 1,000 non-migrants with tuberculosis (1:2) to assess this association.

9.3.1 What are independent and dependent variables? What is their importance?

Variables can be classified as independent (exposure) and dependent (outcome) variables. Independent or exposure variables are expected to cause or influence the dependent or outcome variable. The outcome or dependent variables can be modified based on the status of the independent or exposure variable.

In the migrant and non-migrant study, migration status is the independent (exposure) variable and unsuccessful treatment outcome is the dependent (outcome) variable. As part of the study, we want to assess whether unsuccessful treatment outcome is dependent on the migrant status of a person with tuberculosis. In simple words, we want to see whether there is any difference in the proportions of unsuccessful treatment outcomes between migrants and non-migrants with tuberculosis.

Based on previous research on tuberculosis treatment outcomes, we already know that age, gender, type of case, type of diagnosis, tobacco and alcohol use are independent variables that can affect unsuccessful treatment outcomes. Unsuccessful treatment outcomes can also be influenced by many other independent variables. If the other independent variables are unevenly distributed between migrants and non-migrants, any association between migrant status and the unsuccessful treatment outcomes could be merely due to confounding (as discussed in detail in section 7.7). For example, in case the majority of the migrants with tuberculosis are males and if males have more unsuccessful treatment outcomes, then the higher unsuccessful treatment outcomes among migrants could be merely due to a greater number of males among migrants.

The ability to capture and include all the potential independent variables in the analysis would help to overcome the confounding. Therefore, it is the responsibility of the researcher to identify and capture the list of potential independent variables that can influence the dependent variable (either directly or indirectly) and include them in the research.

Strictly speaking, it is not always feasible to accommodate all independent variables in the study. However, the researcher should brainstorm and identify the most important independent variables and include them in the protocol. Conducting a thorough review of literature, discussion with the experts in the specific field and review of reports and relevant documents will help to identify and include potential independent variables.

9.3.2 What is hypothesis testing?

The concept of hypothesis testing comes into play only in analytical study designs. (7) In analytical studies, the researchers always have a hypothesis at the start of the study and the study is conducted to assess whether the hypothesis has to be rejected or not. There are two types of hypotheses in research.

1. **Null hypothesis** (statistical hypothesis): It is a statement which specifies that there is no difference between the study groups in terms of outcome of interest. The null hypothesis, denoted by "H0", usually indicates that the difference in study observations results purely from chance.
   Example: There is no difference in unsuccessful treatment outcomes among migrants and non-migrants with tuberculosis.

2. **Alternative hypothesis**: The alternative hypothesis, denoted by "H1" or "Ha", is that the sample observations are influenced by some non-random cause. It is a statement which specifies that there is a difference between the study groups in terms of outcome of interest. The directional alternative hypothesis specifies the direction of the difference between the study groups.
   Example: The migrant with tuberculosis have higher unsuccessful treatment outcomes compared to non-migrants with tuberculosis.

All the statistical analysis is based on the null hypothesis. When the null hypothesis is rejected (p value <0.05), it means that the null hypothesis is false. In science, whenever researchers set out to determine whether a true difference exists, they begin with the assumption that there is no difference. To conclude that there is a difference, the task is to reject (disprove) the null hypothesis.

Example: We conduct the study and reveal the following findings as presented in Table 9.2.

Table 9.2 Tuberculosis treatment outcomes among migrants and non-migrants with tuberculosis

Migrant status	Unsuccessful outcome	Successful outcome	Total
	n (%)	n (%)	
Migrant	125 (25)	375 (75)	500
Non-migrant	150 (15)	850 (85)	1,000
Total	275 (18)	1,225 (82)	1,500

It is evident that there is a difference in the percentage with unsuccessful treatment outcomes among migrants (25%) and non-migrants (15%). However, this difference in the percentage that we observe with the study sample is not enough to infer about the difference in percentage in the whole study population. According to the null hypothesis, the difference we have noted in the migrants and non-migrants selected through random sampling could just be due to chance by selecting this sample.

Thus, to be able to infer to the study population (whole of migrant and non-migrant population) based on the findings from this study sample, we need to test the null hypothesis. While testing the null hypothesis, errors are possible as we are always dealing with samples and generalising to populations. There are two kinds of errors – alpha and beta errors. (8)

Table 9.3 Errors in hypothesis testing

Hypothesis testing		TRUTH (Study population)	
		Difference	No Difference
Study sample	Difference	**(1-beta)Power**	**Type I error (alpha error) False Positive error**
	No Difference	**Type II error (beta error) False Negative error**	**(1-alpha) Confidence**

9.3.2.1 What is an alpha error?

The 'alpha error' is the error of commission. It is also called a False Positive (FP) error. It is the probability of falsely stating that there is difference between study groups, when in reality there is no difference between the groups in the study population. Or inversely, the probability of falsely ascertaining an association due to chance when in reality it does not exist. As it is an error of commission and practices can change based on this error, it is essential to keep it below 5% or 0.05. When the alpha error is less than 0.05, we are confident (inverse) that the difference noted is not due to chance and the null hypothesis can be rejected.

Example: Due to the chance of selecting a specific sample, we may falsely conclude that there is an association between migrant status and unsuccessful treatment outcomes when such an association does not exist among the population of migrants and non-migrants with tuberculosis.

9.3.2.2 What is a beta error?

The 'beta error' is the error of omission, also called a False Negative (FN) error. It is the probability of showing no difference between the study groups when in reality there is a difference between the groups in the study population. Or inversely, it is the probability of falsely not ascertaining the association when in reality it does exist. It is an error of omission that could be picked up by another research team. The error of omission is kept at 20% or 0.2. It is often agreed in science that when the beta error is less than 0.2, there is adequate power (inverse) to find a significant difference between groups.

Example: Due to the chance of selecting a specific sample, or not including an adequate sample size, we may falsely conclude that there is no association between migrant status and unsuccessful treatment outcomes, when such an association does exist among the population of migrants and non-migrants with tuberculosis.

9.3.2.3 What is the p value? Is it a measure of inferential statistics?

P value is the probability that the association or difference observed would occur just by chance due to a sampling error alone; it is an estimate of the alpha error. (7) Smaller p values (<0.05) indicate that an association or difference seen is less likely due to chance of sampling. In turn, this enables the null hypothesis to be rejected and a conclusion reached that an association or difference exists in the study population. The smaller the p value, the more confidence there is in rejecting the null hypothesis.

In an analytical study, a univariate analysis can first be conducted to see if there is association between each of the independent and dependent variables. This can be done using the tests of significance and deriving p values.

All the independent variables with p value <0.05 can be considered to be significantly associated with the dependent variable. The p value helps to infer that the difference seen between the study groups not only exists in the study sample but also in the study population.

Example: Unsuccessful outcomes among migrants with tuberculosis are recorded as 125/500 (25%) and among non-migrants as 150/1000 (15%). The p value derived using the Chi-Squared test is <0.001 and indicates that there is a statistically significant difference in unsuccessful outcomes between the two study groups. Thus, we can infer that there is a difference in the unsuccessful outcomes among the migrant and non-migrant populations with tuberculosis.

9.3.2.4 How to choose an appropriate test of significance to derive p values?

The choice of the test of significance to derive p values depends on the following factors:

1. Type of the dependent variables: In most OR studies, the dependent or the outcome variable will be categorical in nature. For example, unsuccessful treatment outcome is a categorical variable. However, it is not always true that all the studies will have a categorical dependent variable. For example, in a study assessing the impact of structured physical activity (yes/no) with the systolic blood pressure, the outcome variable is continuous in nature.

2. The study groups are dependent (repeated measures) or independent: The study groups are considered to be dependent if the same participant has contributed data on the outcome of interest at multiple time points. In such studies, the outcomes are compared across the multiple time points and each time point acts as an exposure category. For example, we assess the systolic blood pressure before-and-after some structured physical activity for 30 minutes, the exposure groups are before and after time points and the outcome is systolic blood pressure. Similarly, we can compare the systolic blood pressure across more than two time points, such as before structured physical activity, one hour after physical activity and six hours after physical activity. In most OR studies, the study groups are independent which means the exposure and outcome variable are measured only once and the study groups are based on the categories in the exposure variable. For example, in the migrant status and unsuccessful treatment outcomes study, the exposure variable and the outcome variable are measured only once. The two study groups, migrants and non-migrants are the categories of the migrant status (exposure variable) and are mutually exclusive and not repeated.

3. The number of categories in the independent variable: In most OR studies, independent variables will be categorical in nature. For example, the migrant status of the people with tuberculosis is a categorical variable with two categories (migrants and non-migrants). Similarly, there may be independent variables, such as depression (No depression, Mild depression, Moderate depression and Severe depression) with more than two categories. Also, studies with repeated measures could have two time points or more than two time points as discussed earlier.

4. If the dependent variable is continuous in nature, there are two more assumptions which need to be checked:

   a. Normal distribution: It is important to check if the outcome variable follows a normal distribution within each of the study groups. For example, if we plan to compare age between migrants and non-migrants with tuberculosis, we need to see whether age is normally distributed among migrants and among non-migrants.

   b. Homogeneity of variance: It is important to check whether the variance of the outcome variable is different between the study groups. For example, if we plan to compare age between migrants and non-migrants with tuberculosis, we need to see whether variance of age is different across migrants and non-migrants.

Once the above elements are checked, then the appropriate test of significance for testing the hypothesis can be selected.

Continuous or discrete variable as the outcome variable

In situations where the continuous or discrete variable is the outcome of interest, it is necessary to choose either a parametric or non-parametric test of significance. The choice of the test depends on normality and homogeneity of variance. Parametric tests can be applied only when the continuous variable follows a normal distribution and the variance is the same across the study groups. The summary measures to be presented when applying parametric tests are the mean with standard deviation and for non- parametric tests, they are the median with interquartile range.

An explanation how to check for normality was presented earlier (in 9.2.1.3) using a rule of thumb. The homogeneity of variance can be checked with the Levene's test for equality of variance using the software packages. The null hypothesis for Levene's test is that 'There is no difference in the variance across the study groups'. If the p value from the Levene's test is < 0.05 and the null hypothesis is rejected, it means that there is a difference in variance. Most of the software packages provide the p value for Levene's test when a parametric test is used.

Once the assumptions have been checked, the appropriate test of significance can be chosen from the table below.

Table 9.4 Parametric and non-parametric tests of significance

Exposure Variable: Type or Variable with number of categories	Parametric test: Outcome variable is continuous and follows normal distribution with homogeneity of variance	Non-parametric test: Outcome variable is discrete or continuous without following normal distribution or without homogeneity of variance
Summary measure presented	Mean with Standard Deviation	Median with Interquartile Range
Comparing across categorical variable with two independent groups	Unpaired t-test or Student's t test	Mann Whitney test or Wilcoxon rank sum test
Comparing across categorical variable two dependent groups (before-and-after)	Paired t-test	Wilcoxon signed-rank test
Comparing across categorical variable with more than two groups	Analysis of variance (ANOVA)	Kruskal-Wallis test
Comparing across categorical variable with more than two dependent groups	Repeated measures of ANOVA	
Exposure variable is continuous variable	Pearson's correlation	Spearman's rank correlation
Exposure variable is discrete variable		Kendal Tau Correlation

Categorical variable as the outcome variable

When the outcome variable is the categorical type, the only test of significance that is used is the Chi-squared test, irrespective of the number of categories in the independent and the dependent variables.

The Chi-squared test is a significance test used to compare the tallies or counts of categorical variables between two (or more) independent groups. It compares observed values against what is expected if the null hypothesis is true. The null hypothesis is that there is no difference between the independent groups in terms of distribution of the outcome variable of interest.

Example: We are interested in knowing if there is an association between migrant status and unsuccessful treatment outcome – see Table 9.5. The obvious question of interest being whether unsuccessful outcome (dependent or outcome variable) differs between the migrant status groups (explanatory variable).

Table 9.5 Tuberculosis treatment outcomes among migrants and non-migrants with tuberculosis

Migrant status	Unsuccessful outcome	Successful outcome	Total
	n (%)	n (%)	
Migrant	125 (25)	375 (75)	500
Non-migrant	150 (15)	850 (85)	1,000
Total	275 (18)	1,225 (82)	1,500

From the data presented in the above table, it is evident that there is a difference in the percentage with unsuccessful treatment outcomes among migrants with tuberculosis (25%) and non-migrants with tuberculosis (15%). The question that rises is whether this difference is due to chance. Each of the values in the table is subject to sampling error and we need some way of assessing whether the difference between them is a 'true' difference or just due to chance. Thus, need to use Chi-squared test for testing the null hypothesis.

The Chi-squared test derives a p-value of <0.001. This means we can reject the null hypothesis. We can state that there is a statistically significant difference in unsuccessful outcomes across the migrant status groups or there is a statistically significant association between migrant status groups and unsuccessful outcomes. However, the p-value will not be able to tell how big this difference between the groups is. This can be derived from the measures of association.

9.3.3 What are measures of association?

The measures of association are a wide variety of statistics that quantify the strength and direction of the relationship between independent (exposure) and the dependent (outcome) variables. (9) The measure of association depends on the study design used to collect the data. The study designs and the appropriate measure of association when the outcome variable is of the categorical type is shown in Table 9.6.

Table 9.6 Study designs and related measures of association

Study design	Measure of association
Cohort study	Relative Risk or Risk Ratio
Case-control study	Odds Ratio (Exposure Odds Ratio)
Cross-sectional analytical study with outcome of interest more than or equal to 10%	Prevalence Ratio
Cross-sectional analytical study with outcome of interest less than 10%	Prevalence Ratio or Odds Ratio (Diseases Odds Ratio)

9.3.3.1 What is relative risk?

The relative risk (also called the risk ratio, RR) is the ratio of the risk of an event or outcome of interest in the exposure group to the risk of the event or outcome of interest in a comparative group (non-exposure or control group). The relative risk is calculated as the measure of association in cohort studies. As cohort studies include follow-up, they will be able to provide the risk (probability) of developing the outcome of interest in the exposure group and the non-exposure group.

Calculation of relative risk

When the table for calculating the measure of association is constructed, the exposure categories will be in the rows and the outcome categories will be in the columns. The first row will ideally have the exposure of interest and the first column will be the outcome of interest.

Example: In table 9.7, the exposure of interest is migrant status and the outcome of interest is unsuccessful tuberculosis treatment outcome. We plan to compare the risk of unsuccessful outcome in migrants with tuberculosis (exposed group) to non- migrants with tuberculosis (non-exposed group).

Table 9.7 Tuberculosis treatment outcomes among migrants and non-migrants with tuberculosis

Migrant status	Unsuccessful outcome n (%)	Successful outcome n (%)
Migrant	125 (25) (a)	375 (75) (b)
Non-migrant	150 (15) (c)	850 (85) (d)
Total	275 (18)	1,225 (82)

- Risk of unsuccessful outcome in migrants = a/(a+b) = 125/500 = 0.25 (25%)

- Risk of unsuccessful outcome in non-migrants = c/(c+d) = 150/1000 = 0.15 (15%)

- Relative risk or risk ratio = 0.25/0.15 = 1.7

Interpretation of relative risk

According to the study sample, the risk of unsuccessful outcome among the migrants with tuberculosis is 1,7 times the risk among the non-migrants with tuberculosis. The relative risk (RR) can be interpreted as follows:

- RR of 1: No difference in risk between the two groups (Null value)

- RR > 1: A "greater risk" of developing the event in the exposure group

- RR < 1: A "lower risk" ("protective effect") of developing the event in the exposure or intervention group

As the relative risk is more than 1 in the example, we can conclude that there is a higher risk of unsuccessful treatment outcome among migrants with tuberculosis compared non-migrants with tuberculosis in the study sample.

As the relative risk increases, each incremental increase of 0.1 is the equivalent of a 10% increase in risk in the intervention or exposed group compared to the control or non-exposed group. In the example with the relative risk of 1.7 suggests that migrants with tuberculosis have 70% greater risk of unsuccessful outcomes than non-migrants with tuberculosis.

As the relative risk decreases, each incremental decrease of 0.1 is the equivalent of a 10% decrease in risk in the intervention or exposed group compared to the control or non-exposed group. If the relative risk of diarrhoea among infants that are exclusively breastfed (exposed group) compared to infants that are not exclusively breastfed (non-exposed group) is 0.8, it means that the infants that are exclusively breastfed have 20% less risk of diarrhoea.

Inferential statistics with 95% confidence interval for relative risk

The relative risk as such is a summary statistic and does not provide an estimate about the risk in the study population. Thus, we need to calculate the 95% confidence interval for the relative risk to get an estimate of risk in the migrant population with tuberculosis compared to non-migrant population with tuberculosis.

The relative risk (95% CI) for the above example is 1.7 (95% CI: 1.3 – 2.1). With 95% confidence, we can see that the risk of unsuccessful outcome among the migrants with tuberculosis is between 1.3 and 2.1 times that among the non-migrants with tuberculosis. As the range of 95% confidence interval does not include the null value of 1 ('no difference') and both the lower and higher limits are above 1, we can be 95% confident that the risk of unsuccessful outcome is significantly higher in the migrant population with tuberculosis compared to the non-migrant population with tuberculosis. The p value will be below 0.05.

Conversely, if the 95% confidence interval does not include the null value of 1 and both the lower and higher limits are below 1, we can be 95% confident that the risk of outcome of interest is significantly lower in the exposure group compared to non-exposure group. The p value will be below 0.05. If the 95% confidence interval includes the null value of 1, then there is no statistically significant difference between the study groups. Thus, we are not able to confidently tell whether the risk in the exposure group is higher or lower than that in the non-exposure group.

9.3.3.2 What is an Odds Ratio?

The classical Odds Ratio from a case-control study is the ratio of the odds of an exposure in the case group compared to the odds of exposure in the control group. Odds is a concept that is more familiar to gamblers. The odds is the ratio of the probability that a particular event will occur to the probability that it will not occur. It can be any number between zero and infinity. In a case-control study, the researcher calculates the odds of exposure in the case group and the odds of exposure in the control group.

Calculation of Odds Ratio

As for other tables for calculating the measure of association, the exposure categories will be in the rows and the outcome categories will be in the columns. The first row will ideally have the exposure of interest and the first column will be the outcome of interest.

Example: Let us assume that a case-control study was conducted with inclusion of cases-unsuccessful outcomes and controls (which in this case are successful outcomes) to see if the outcomes are associated with migrant status (Table 9.8). It follows that the exposure of interest is migrant status and the outcome of interest is unsuccessful tuberculosis treatment outcome. We plan to compare the odds of exposure (migrant status) in those with unsuccessful outcomes to those with successful outcomes.

Table 9.8 Calculation of Odds Ratio in a study on tuberculosis treatment outcomes among migrants and non-migrants with tuberculosis

Migrant status	Unsuccessful outcome	Successful outcome	Total
	n (%)	n (%)	
Migrant	125 (25) (a)	375 (75) (b)	500
Non-migrant	150 (15) (c)	850 (85) (d)	1,000
Total	275 (18)	1,225 (82)	1,500

- Odds of exposure among those with unsuccessful outcome = a/c = 125/150 = 0.83

- Odds of exposure among those with successful outcome = b/d = 375/850 = 0.44

- Odds Ratio = 0.83/0.44 = 1.9

Interpretation of Odds Ratio

According to the study sample, the odds of migrant status (exposure) among those with unsuccessful outcome is 1.9 times that of the odds of migrant status (exposure) among those with successful outcome. The Odds Ratio can be interpreted as follows:

- OR of 1: No difference in exposure between the cases and controls (Null value)

- OR > 1: The cases have higher odds of exposure compared to the controls

- OR < 1: The cases have lower odds of exposure compared to the controls

As the Odds Ratio is more than 1 in the example, we can conclude that there is a higher odds of exposure among those with an unsuccessful outcome compared to those with a successful outcome.

In case-control studies, the exposure Odds Ratios are calculated. However, with cross-sectional analytical studies, we can calculate the disease Odds Ratios. The disease Odds Ratios are the ratio of odds of disease among the exposed over the odds of disease among the unexposed. Mathematically both exposure Odds Ratios and disease Odds Ratios are same. However, they need to be interpreted differently. In case we calculated a disease Odds Ratio of 1.9 in the above example, the interpretation would be as follows: odds of unsuccessful outcomes among the migrants is 1.9 times that of the odds of unsuccessful outcomes among non-migrants. As noted, the Odds Ratios overestimate the measure of association compared to relative risk.

Thus, these measures of association are not preferred in cohort and cross-sectional study designs.

Inferential statistics with 95% confidence interval for Odds Ratio

The Odds Ratio is a summary statistics and does not provide the estimate about the extent of exposure in the population of cases and controls. We need to calculate the 95% confidence interval for the Odds Ratio to estimate the extent of exposure in the population with unsuccessful and successful outcomes.

The Odds Ratio (95% CI) for the above example is 1.9 (95% CI: 1.4 – 2.5). With 95% confidence, we can tell that the odds of exposure among those with unsuccessful outcome is between 1.4 and 2.5 times higher than that in the successful outcome population. As the range of 95% confidence interval does not include the null value of 1 and both the lower and higher limits are above 1, we can be 95% confident that the odds of exposure is significantly higher in the unsuccessful outcome population compared to successful outcome population. The p value will be below 0.05.

If the 95% confidence interval does not include the null value of 1 and both the lower and higher limits are below 1, we can be 95% confident that the exposure is significantly lower in the case group compared to the control group. The p value will be below 0.05. If the 95% confidence interval includes the null value of 1, then there is no statistically significant difference between the case and control groups. Thus, we are not able to tell confidently whether the exposure is higher or lower in the case group compared to the control group.

9.3.3.3 What is prevalence ratio?

The prevalence ratio (PR) is the ratio of the prevalence of an event or outcome of interest in the exposure group of interest to the prevalence of the event or outcome of interest in the comparative group (non-exposure or control group). The prevalence ratio is calculated as the measure of association in cross-sectional studies. As cross-sectional studies include assessment of both the exposure and outcome of interest at the same time point, the probability of having the outcome of interest (prevalence) in the exposure group and the non-exposure group can be calculated.

Calculation of prevalence ratio

As in other tables for calculating measures of association, the exposure categories will be in the rows and the outcome categories will be in the columns. The first row will ideally have the exposure of interest and the first column will be the outcome of interest. Let us assume that a cross-sectional study was conducted to assess the association between tobacco use and diabetes disease status.

Example: The exposure of interest is tobacco use and the outcome of interest is diabetes. We plan to compare the prevalence of diabetes among those who use tobacco and among those who do not use tobacco (Table 9.9).

Table 9.9 Calculation of prevalence ratio in a cross-sectional study on association tobacco use and diabetes

Tobacco use	Diabetes	No diabetes	Total
	n (%)	n (%)	
Yes	125 (25) (a)	375 (75) (b)	500
No	150 (15) (c)	850 (85) (d)	1,000
Total	275 (18)	1,225 (82)	1,500

- Prevalence of diabetes among those with tobacco use = a/(a+b) = 125/500 = 0.25 (25%)
- Prevalence of diabetes among those without tobacco use = c/(c+d) = 150/1,000 = 0.15 (15%)
- Prevalence ratio = 0.25/0.15 = 1.7

Interpretation of prevalence ratio

According to the study sample, the prevalence of diabetes among those with tobacco use (exposure) is 1.7 times higher than the prevalence of diabetes among those without tobacco use. The prevalence ratio can be interpreted as follows:

- PR of 1: No difference in prevalence of disease between the study groups (Null value)
- PR > 1: A "greater risk" of having the disease in the exposure group
- PR < 1: A "lower risk" ("protective effect") of having the disease in the exposure group

As the prevalence ratio is more than 1 in the example, we can conclude that there is a higher prevalence of diabetes among those with tobacco use compared to those without tobacco use.

The prevalence ratio and relative risk are mathematically the same. However, the interpretation differs. The relative risk provides the risk of developing the disease (incidence) in the exposure group, whereas the prevalence ratio provides the measure of association of having the disease (prevalence) in the exposure group.

Inferential statistics with 95% confidence interval for prevalence ratio

The prevalence ratio is the summary statistic and does not provide the estimate of the relative prevalence of disease in the population of the exposure group compared to the population of the non-exposed group. Thus, we need to calculate the 95% confidence interval for the prevalence ratio.

The prevalence ratio (95% CI) for the above example is 1.7 (95% CI: 1.3 – 2.1). With 95% confidence, we can see that the prevalence of diabetes among the tobacco use population is between 1.3 and 2.1 times that in the non-tobacco use population. As the range of 95% confidence interval does not include the null value of 1 and both the lower and higher limits are above 1, we can be 95% confident that the prevalence of diabetes is significantly higher in the tobacco use population compared to no tobacco use population. The p value will be below 0.05.

If the 95% confidence interval does not include the null value of 1 and both the lower and higher limits are below 1, we can be 95% confident that the prevalence of disease is significantly lower in the exposure population compared to the non-exposure population. The p value is below 0.05. If the 95% confidence interval includes the null value of 1, then there is no statistically significant difference between the exposure population and the non-exposure population. Thus, we are not able to confidently tell whether the disease is higher or lower in the exposure population compared to the non- exposure population.

9.3.3.4 What is mean difference?

When the outcome variable is continuous in nature, the mean difference can be used as the measure of association. In Table 9.10, we assess the difference in age between the migrants and non-migrants with tuberculosis included in the study.

Table 9.10 Calculation of mean difference in a study on age distribution between migrants and non-migrants with tuberculosis

Variable	Migrants, N=500 Mean (SD)★	Non-migrants, N=1,000 Mean (SD)★	Mean Difference (95% CI)★	P Value
Age in completed years	44 (17)	39 (18)	5 (3.1 – 6.9)	<0.001

★SD = Standard Deviation, CI = Confidence Interval

The mean difference in the age between migrants and non-migrants with tuberculosis included in the study is 5 years. With 95% confidence, we can tell that the mean difference in the whole population of migrants and non-migrants with tuberculosis lies somewhere between 3.1 and 6.9 years. The migrants with tuberculosis have a higher age (are older) compared to the non-migrants with tuberculosis as the 95% confidence interval does not include the null value of 0.

9.3.3.5 What is confounding and how to limit its effect?

Confounding in research is the mixing of the effect of the exposure under study on the disease (outcome) with that of a third factor that is associated with the exposure and is an independent risk or prognostic factor for the disease. (10) The consequences of confounding are the overestimation or underestimation of the true association between the exposure and outcome under study. The concept of confounding has been discussed detail in 7.7. This section explains how to address the effect of confounding at the time of analysis.

Example: In the study assessing association of migrant status with unsuccessful tuberculosis treatment outcomes, we already know that age, gender, type of case, type of diagnosis, tobacco and alcohol use are independent variables that can affect the unsuccessful treatment outcomes. In case of migrants, majority of those with tuberculosis are males and if males have higher unsuccessful treatment outcomes, then the high unsuccessful treatment outcomes among migrants could merely be due to more males among migrants (Figure 9.4).

Figure 9.4 Diagram representing the confounding effect of gender on the tuberculosis treatment outcomes
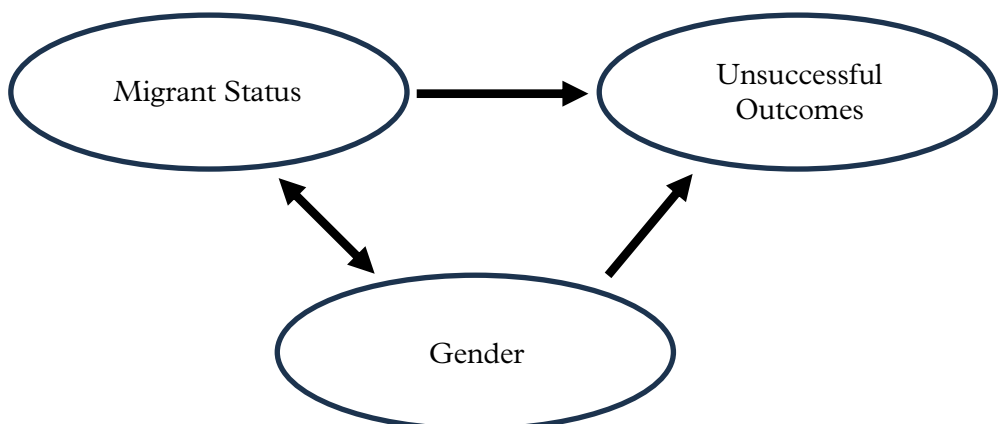
Controlling for confounding

Confounding can be controlled in the study design (randomisation, restriction and matching) and in the study analysis (stratification, multivariable analysis and matching).

i) **Study design**: A factor can confound an association only if it differs between the study groups. This is the basis for the following methods to control confounding in the study design:

1. Randomisation: Ensures that potential confounding factors, known or unknown, are evenly distributed among the study groups. Note that randomised controlled studies are the best design for controlling known and unknown confounders.

2. Restriction: Restricts admission to the study to a certain category of a confounder.

3. Matching: Equal representation of subjects with certain confounders among study groups.

ii) **Study analysis**: Methods used to control for confounding at the analysis stage include stratified analysis and multivariable analysis that produce adjusted estimates of the size of the effect. Based on the type of outcome variable, the study design and the measure of association that is desired, multivariable regression can be used for adjusting confounders (Table 9.11).

Table 9.11 Type of outcome and measure of association using regression method

Type outcome variable	Study design	Measure of association	Regression method to be used
Continuous	Any analytical design	Beta Coefficient	Multivariable linear regression
Categorical (Binary)	Cohort study	Relative Risk	Multivariable log binomial regression OR Modified Poisson regression
Categorical (Binary)	Case-control study	Odds Ratio	Multivariable logistic regression OR Conditional logistic regression (11)
Categorical (Binary)	Cross-sectional study	Odds Ratio	Multivariable logistic regression
Categorical (Binary)	Cross-sectional study	Prevalence Ratio	Multivariable log binomial regression OR Modified Poisson regression (11)
Count Data (Discrete)	Cohort or Cross-sectional study	Incidence Rate Ratio	Poisson regression
Time-to-event	Cohort study	Hazard Ratio	Cox proportional-hazards model

Example: in a study assessing the association of migrant status with unsuccessful treatment outcomes, we can include all the potential independent variables in the multivariable log binomial regression and calculate the adjusted relative risk with 95% confidence interval for migrants with tuberculosis compared to non-migrants with tuberculosis. This provides the independent effect of the migrant status on the unsuccessful treatment outcomes after adjusting for the known confounders.

As these are explanatory multivariable regressions, we can include all the variables into the model.

However, if there are sample size constraints, we can include only the independent variables which are significant (p value <0.05) or those with p value <0.2. The decision on the cut-off of the p value can be taken based on the sample size. Ideally, we can have one independent variable with two categories included in the multivariable model for every 10 outcomes of interest.

Example: As there are 225 individuals with unsuccessful treatment outcomes in our study example, we can include up to 22 independent variables with binary categories. If there are independent variables with 5 categories, it is almost as including four independent variables into the multivariable regression.

Also, it is important to check for multi-collinearity between the independent variables. Multi-collinearity is a statistical concept where several independent variables in a multivariable model are correlated. (12) The inclusion of independent variables which are collinear in the multivariable model can reduce the power of the regression analysis. Thus, it is important to check for multi-collinearity between the independent variables included in the multivariable model and exclude some collinear variables. To detect multi-collinearity in the multivariable model, the software packages can give a numerical value called variation inflation factor (VIF) for each of the independent variables. The independent variables with VIF of >5 can be excluded from the final model to improve the power of the analysis when the sample size is small. If the sample size is large, all the independent variables can be included in the final multivariable analysis.

9.3.4 How to draft the data analysis plan for analytical study?

In the OR protocol, the data analysis plan has to be described under the methods section. It is important to highlight the items below:

1. The software and version that will be used for data entry and analysis.

2. The summary statistics that will be used for summarising all the independent variables and dependent variables included in the study.

3. In studies assessing the association between a specific independent (exposure) and the dependent (outcome) variable, the hypothesis tests that will be used to compare other independent variables across the exposure groups. This is to see if other independent variables are evenly distributed across the exposure groups.

4. The hypothesis test that will be used to compare the dependent variables across the categories of independent variables.

5. Regression methods that will be used to derive the appropriate measure of association with 95% CI to assess the effect of independent variables on the outcome variable after adjusting for confounders (if the sample size permits such exploration).

Example: For an OR study conducted to assess whether there is any association between migrant status and unsuccessful treatment outcomes among people with pulmonary tuberculosis initiated on treatment during 2022 in the city X, the data analysis plan is provided below.

"Data will be double entered and validated using EpiData entry version 3.1 (EpiData Association, Odense, Denmark). The analysis will be conducted using Stata 11.0 (StataCorp LP, College Station, TX, USA).

All summary statistics will be calculated stratified by the migrant status. Categorical variables like gender, type of case, type of diagnosis, tobacco use and alcohol use will be summarised using frequency and proportions. Age in completed years will be summarised using mean with standard deviation or median with interquartile range based on the normal distribution. The number of household contacts will be summarised using median with interquartile range.

Categorical variables like gender, type of case and type of diagnosis will be compared across the migrant status (migrants and non-migrants) categories using the Chi- Squared test. Age in completed years will be compared across migrant status using the unpaired t test or Mann Whitney U test, based on the normal distribution and homogeneity of variance. The number of household contacts will be compared across the migrant status groups using the Mann Whitney U test. P value < 0.05 will be considered as statistically significant.

The programmatic tuberculosis treatment outcomes will be converted into binary categories of unsuccessful and successful treatment outcomes. The unsuccessful treatment outcomes will include death, lost to follow-up, failure and not evaluated. The successful treatment outcomes will include cured and treatment completed. The frequency and percentage with 95% Confidence Interval (CI) will be used as summarise the unsuccessful treatment outcomes. The distribution of unsuccessful treatment outcomes will be compared across the migrant status (migrants and non-migrants) categories using Chi- Squared test.

In case of a significant difference in the distribution of unsuccessful outcomes across the migrant status categories, the independent effect of migrant status on the unsuccessful outcomes will be assessed using multivariable regression analysis. Multivariable log binominal regression will be conducted with inclusion of all the independent variables included in the study. The multi-collinearity between the independent variables will be assessed and the variables with a variation inflation factor >5 will be excluded from the regression model. The adjusted relative risk with 95% CI will be calculated as the measure of association."

References

1. NIH Library. Common Data Types in Public Health Research | NIH Library [Internet]. 2023 [accessed 25 August 2023]. Available from: https://www.nihlibrary.nih. gov/resources/subject-guides/health-data-resources/common-data-types-public- health-research

2. Guetterman TC. Basics of statistics for primary care research. Fam Med Community Heal. 2019; 7(2): e000067.

3. Simpson SH. Creating a data analysis plan: What to consider when choosing statistics for a study. Can J Hosp Pharm. 2015; 68(4):311-7.

4. Grimes DA, Schulz KF. Descriptive studies: What they can and cannot do. Lancet. 2002; 359(9301):145–9.

5. Ghasemi A, Zahediasl S. Normality tests for statistical analysis: A Guide for non-statisticians. Int J Endocrinol Metab. 2012; 10(2): 486-9.

6. Greenland S, Senn SJ, Rothman KJ, et al. Statistical tests, P values, confidence intervals and power: a guide to misinterpretations. Eur J Epidemiol. 2016; 31(4):337-50.

7. Shreffler J, Huecker MR. Hypothesis testing, P values, confidence intervals and significance. StatPearls. 2023.

8. Banerjee A, Chitnis UB, Jadhav SL, Bhawalkar JS, Chaudhury S. Hypothesis testing, type I and type II errors. Ind Psychiatry J. 2009;18(2):127-31.

9. Gallis JA, Turner EL. Relative measures of association for binary outcomes: Challenges and recommendations for the Global Health Researcher. Ann Glob Heal. 2019; 85(1): 137.

10. Grimes DA, Schulz KF. Bias and causal associations in observational research. Lancet. 2002; 359(9302): 248–52.

11. UCLA Statistical Methods and Data Analytics. How can I estimate relative risk using glm for common outcomes in cohort studies? | Stata FAQ [Internet]. [cited 25 August 2023]. Available from: https://stats.oarc.ucla.edu/stata/faq/how-can-i-estimate-relative-risk-using-glm-for-common-outcomes-in-cohort-studies/

12. Vatcheva KP, Lee M, McCormick JB, McCormick JB, Rahbar MH. Multicollinearity in regression analyses conducted in epidemiologic studies. Epidemiol. 2016; 6(2):227.

10 Monitoring operational research

This chapter provides an overview of the importance of monitoring the implementation of OR and tools to carry this out. The chapter also highlights the mechanisms that the investigators can adopt for quality assurance of OR.

10.1 Is monitoring important in OR?

OR seeks to transform data (from primary or secondary sources) into useful information about how the health system works and use that evidence for decision making to improve public health. (1) While a well conducted OR can contribute to significant improvements in programme performance, poorly conducted OR can do more harm than good.

It is therefore important to monitor any OR study through regular, systematic and purposeful observation and recording of activities to:

- Ensure compliance to the protocol

- Ensure integrity and quality of data

- Ensure timely conduct of the study so that the results are disseminated to policy makers within the timeframes for decision-making

- Ensure ethical conduct of research

- Identify roadblocks and troubleshoot or do mid-course corrections

10. 2 How can OR be monitored?

OR utilises frequently data which is routinely collected as part of the health programmes. In these studies, the element of monitoring from the ethical perspective may not be very relevant. However, when the data is being extracted from paper-based registers and records, it is necessary to monitor the timeliness and completeness of the data extraction.

When OR is carried out using primary data collection, it is essential to monitor the study procedures in terms of ethical perspective, timelines and quality of data collection. This type of research is more labour-intensive and demanding than research using routinely collected health programme data. Certain aspects of OR can be monitored remotely and certain aspects require on-site monitoring. Either way, it is advisable to develop a plan for monitoring and conduct regular team meetings to discuss the observations made as part of monitoring and plan for further action.

Remote monitoring

Remote monitoring of OR can be done by a designated central coordinating team. This is particularly relevant in multi-centric studies. Remote monitoring involves:

- Periodic data quality checks and analysis

- Monitoring progress of the study against timelines envisaged in the protocol

- Keeping track of the study related expenditures against the available funds.

On-site monitoring

Wherever feasible, provisions for on-site monitoring should be built into the research protocol and budget. On-site monitoring involves visits to study sites for the purpose of:

- Checking if fidelity to the study procedures is maintained by all study teams and in all study sites

- Inspecting completeness and correctness of the study related documents, such as case report forms and informed consent documents

- Validating the study data with the source documents, such as tuberculosis registers

- Resolving queries of field teams or undertaking troubleshooting in case of electronic data capture processes.

10. 3   How can an investigator build in quality assurance and control mechanisms within OR?

Quality assurance (QA) refers to all steps taken to ensure that data are recorded, analysed and recorded in accordance with the protocol and prevailing ethical and scientific quality standards. A subset of QA activities is quality control (QC) which refers to the real time ("day-to-day") observation and documentation of the work processes to ensure that the data generated during the implementation of OR are complete, accurate

and consistent with the study protocol. In other words, QA is about preventing problems from happening, while QC is about detecting and correcting problems that do occur. They are interlinked processes.

These concepts originated from the industrial sector and have rapidly spread to other disciplines. In the field of health research, QA and QC are an integral part and a mandatory regulatory requirement for the conduct of clinical trials. Of late, these concepts are being built into non-interventional studies.

Study protocol

One of the most important steps in quality assurance is development of a detailed and scientific research protocol. The components of an OR protocol have been discussed in the previous chapters. A well-written protocol should include a detailed plan for monitoring the implementation of the OR study.

Adherence to standard reporting guidelines

Standard reporting guidelines are now available for almost all kinds of study designs and can serve as useful tools to ensure that all aspects are taken into consideration during the planning, conduct and reporting of OR. The Enhancing the QUAlity and Transparency Of health Research (EQUATOR) Network is an international initiative that seeks to improve the reliability and value of published health research literature by promoting transparent and accurate reporting and wider use of robust reporting guidelines (available at https://www.equator-network.org/). (2) Examples of reporting guidelines which are commonly applicable to OR studies include Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and Consolidated criteria for reporting qualitative research (COREQ) guidelines. (3,4)

Develop a quality assurance plan

The validity of any OR study is determined almost entirely by the quality of its data. It is useful to breakdown the process of conducting OR into smaller steps as proposed in the "Open Quality Approach" for epidemiology. (5) Doing this exercise at the start of OR is useful as the research team will be able to anticipate and tackle quality issues as the study progresses. All the components listed may not be applicable at all steps.

- Failure modes: What can go wrong?
- Data quality attributes: Which data quality attribute(s) will be affected? Data quality attributes include completeness, accuracy, credibility, timeliness, accessibility, interpretability and coherence. (6)
- Standards/criteria: How can we determine if we have fulfilled the attribute?
- Preventive strategies: How can we prevent things from going wrong and ensure we fulfil the attribute?

- Verification activities: How can we check whether we are on track to fulfil the attribute?

- Corrective actions: What should we do to correct things if we are not on track? How can we prevent it from happening again?

Example: Assume that an OR study is being conducted to list household contacts of persons with pulmonary tuberculosis, screen the contacts for symptoms of tuberculosis, evaluate them for the presence of tuberculosis and initiate tuberculosis preventive treatment whenever applicable. The field team is expected to interact with each person with pulmonary tuberculosis when they are initiated on treatment and line-list their household contacts. Next, they are expected to screen all the listed contacts for symptoms suggestive of tuberculosis during home visits. Symptomatic contacts are evaluated for tuberculosis and started on tuberculosis treatment, if diagnosed with the disease. Those contacts who are asymptomatic or in whom tuberculosis is ruled out are initiated on tuberculosis preventive treatment.

The text box below shows an approach to QA for errors that can occur during the process of line-listing.

Failure modes (What can go wrong?)	Only household members available at the time of home visit are listed as contacts
Data quality attributes (Which data quality attribute will be affected if this goes wrong?)	Completeness and interpretability
Standards/criteria (How can we determine if we have fulfilled the attribute?)	All household contacts should be listed and in case some of them are not available at the time of home visits, this should be noted in the CFRs. Compare the number of contacts enumerated per index patient with the available literature on average family size in the region. These should match.
Preventive strategies (How can we prevent things from going wrong and ensure we fulfil the attribute?)	Make provisions to record total number of household contacts listed for each index patient and include a field in the CRF to capture whether or not a listed contact was available for interview.

Provide timely feedback to teams

Schedule periodic meetings with the field team and ensure that any issues identified during the quality assurance activities are discussed and resolved.

References:

1. Zachariah R, Harries AD, Ishikawa N, et al. Operational research in low-income countries: what, why, and how? Lancet Infect Dis. 2009; 9(11):711–7.

2. EQUATOR Network. Enhancing the QUAlity and Transparency of Health Research [Internet]. 2023 [accessed 25 August 2023]. Available from: https://www.equator-network.org/

3. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007; 370(9596):1453–7.

4. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Heal Care. 2007; 19(6):349–57.

5. Alba S, Straetemans M. Whatever can go wrong, need not go wrong: Open Quality approach for epidemiology. Emerg Themes Epidemiol. 2021; 18: 8.

6. OECD. Quality Framework for OECD Statistical Activities [Internet]. 2023 [accessed 25 August 2023]. Available from: https://www.oecd.org/sdd/ qualityframeworkforoecdstatisticalactivities.htm

11   Communication of operational research findings

This chapter provides an overview of the importance, ways and timing of disseminating findings of an OR study.

11.1 What is the role of communication in OR?

The overall goal of OR is to improve the delivery of health services through identifying challenges or problems in the system, scientifically investigating which factors are related to the challenges and if possible, also identifying why those challenges exist and making recommendations to address them. OR can lead to lasting changes in programmes and it can also result in policy changes, provided the results are communicated to the right persons at the right time. (1)

Although OR is usually context specific, researchers from other programmatic settings may also benefit from learning about its methodology and results. It is, therefore, important to ensure that any OR is disseminated widely within the scientific community.

11.2 How are OR findings disseminated for impacting policy or practice?

Dissemination activities must be selected based on the type of the stakeholder that they are intended for. Stakeholders have been defined as "individuals, organisations or communities that have a direct interest in the process and outcomes of a project, research or policy endeavour". (2) They include policy-makers, programme managers, service providers, programme beneficiaries and donors. It is advisable to develop a dissemination plan with the components listed below. (3) Remember that the plan may need to be adapted to changing circumstances.

- What are the key messages that need to be communicated?
- Who are the stakeholder(s) relevant to this OR?
- Who is the most suitable person to communicate with this stakeholder(s)?
- What are the methods to engage with this stakeholder(s)

- When and where should dissemination activities be planned for this stakeholder(s)?

- What are the ways in which the identified stakeholder(s) may facilitate or hinder the uptake of OR?

Researchers may frequently strive for a publication in a scientific journal as an endpoint of their research. However, in the context of OR it is important to understand that engaging with policy makers to ensure uptake of research findings is equally or perhaps even more important than publishing the findings. The following are ways of disseminating research findings, some of which are discussed in further detail in subsequent chapters:

- Publication in a scientific journal

- Presentation of research findings at national and international conferences

- Press releases and briefings

- Social media posts (Twitter, Facebook, LinkedIn, Academia, etc.) and podcasts

- Dissemination through personal blogs: Tumblr, Wordpress, Research blogging

- Meetings with local and national stakeholders to discuss research findings, with circulation of policy briefs and evidence summaries in plain language

- Regular reports to the funding agency.

11.3 When should OR findings be communicated?

Study findings are communicated during the implementation of the OR or after its completion.

During the OR: It is worthwhile to engage all stakeholders from the beginning of any OR because this fosters a sense of ownership and responsibility, which is key to bringing about change in policy and/or practice. Stakeholders must also be involved in the development of the protocol. They must be kept regularly updated about the progress of OR and the key findings. This can be operationalised by scheduling periodic review meetings to which key stakeholders are invited. However, researchers should keep in mind that early results may be misleading and create false expectations.

After completion of OR: The presentation of results also needs to be timed for when they are most likely to be used. For example, it is good to ensure that the results are communicated to decision makers before the annual programme budget is finalised. This provides an opportunity for changes proposed in the programme (based on OR) to be budgeted for and implemented without undue delay.

These approaches are discussed in detail in the next chapters.

References

1. Zachariah R, Harries AD, Ishikawa N, et al. Operational research in low-income countries: what, why, and how? Lancet Infect Dis. 2009; 9(11):711–7.

2. Deverka PA, Lavallee DC, Desai PJ, et al. Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. J Comp Eff Res. 2012; 1(2):181–94.

3. UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, Global Fund to Fight AIDS, Tuberculosis and Malaria, United Stated Agency for International Development, UNAIDS, World Bank. Framework for operations and implementation research in health and disease control programs [Internet]. World Health Organization; 2008 [accessed 24 August 2023]. Available from: https://apps.who.int/iris/handle/10665/44686

12 Communicating operational research findings through scientific publications

This chapter covers issues, such as the importance of publication, the selection of a journal, writing and preparing a manuscript for submission to a journal, the process of submission, how to handle peer review and manuscript revision and the final steps needed between acceptance and publication of the manuscript.

12.1 Why is publication important?

There is an ancient Roman column standing in the city of Rome inscribed with four Latin words "Scripta manent, verba volant" – "spoken words fly away, written words remain". Two thousand years later, the famous 20th century English writer, Virginia Woolf, is credited with saying "If you do not write about it, it did not happen". Famous people, such as Alexander the Great, Mahatma Gandhi and Nelson Mandela, have ensured that their journeys through life and their achievements have been well documented either by themselves or professional chroniclers. Thus, the need to publish OR. We highlight the key reasons below.

Table 12.1 Reasons for publishing operational research

•	Quality control standard of the OR project
•	Critical way to disseminate and share knowledge and experiences
•	Evidence base for policy change and for local/ national / international policy guidelines
•	Enhances credibility of authors and their institutions
•	Promotes accountability to programme stakeholders and donors

Writing up an OR project for a scientific journal and exposing it to a rigorous peer review is an exacting and labour-intensive activity. The aim and objectives of the research study have to be well articulated and the research data have to be cleaned, analysed and interpreted. The key findings have to be explained within the context of what is already known and published and finally, these findings have to be assessed in terms of what they mean for policy and practice. Properly performed peer review usually improves the scientific rigour and the readability of the manuscript. The published article facilitates the dissemination and sharing of knowledge, it adds to the evidence base on that particular subject and it can underpin the formulation of local, national or international policy guidelines for health.

Despite these good reasons for publishing operational or other types of research in scientific journals, there is a huge amount of research waste. Previous reviews have shown that about 50% of research studies are never published in full. (1) The reasons which are cited include lack of time, motivation, perseverance and opportunity, inadequacies of study design, poor quality of data, lack of support from supervisors and lack of funding or infrastructure. (2) In particular, publications from work at the programme level remain limited and this situation needs to change. Programme researchers in Uganda summarise it well: "If you don't publish articles from your programme or research project, you have not accounted well enough". (3)

12.2 How to select a suitable journal?

The first step in the pathway to publication is to identify the most appropriate journal in which to publish the work. Choosing the journal before you start makes sure that you can follow author guidelines from the beginning and do it right. The important criteria for choosing a journal are summarised below.

Table 12.2 Criteria for choosing a journal

• The audience that the journal addresses and the interests of that journal
• Whether the journal is listed on PUBMED and can be accessed in MEDLINE
• Impact factor
• Turn-around-time
• Open access or closed access
• Previous experience
• Recommendations from a medical librarian or seasoned colleague

The journal's interests: The interests of the journal, the readership and audience to whom the article is primarily directed are important first criteria for choosing a journal. There are many general medical journals with the top ranked ones being the Lancet and the New England Journal of Medicine. There are disease specific journals focusing on communicable diseases, such as the International Journal of Tuberculosis and Lung Disease, AIDS and the Malaria Journal or on non-communicable diseases, such as Diabetes and the Journal of Hypertension. Finally, there are journals focused on OR, The Union's Public Health Action being a prime example.

PubMed listing: The journal must be listed on PubMed which is a free search engine accessing the MEDLINE database of references and abstracts on life sciences and biomedical topics. The United States National Library of Medicine at the National Institutes of Health maintains the database. As of 2022, the MEDLINE bibliographic database contained more than 29 million references to journal articles in life sciences with a concentration on biomedicine, from over 5,000 journals in 40 languages. Being listed on PubMed means that the published article can be identified when other researchers conduct searches on your particular topic.

Impact factor: A journal's impact factor is calculated by dividing the number of times the journal articles are cited in the previous two years by the total number of articles published in those two years. Impact factor is often used to measure the relative importance and rank of a scientific journal within its field: journals with higher impact factor values carrying more prestige than those with lower values. It is also often used by universities and funding bodies to decide on promotion and research proposals. However, the impact factor has been criticised for distorting good scientific practices and in OR it is not highly valued as a metric for choosing a journal.

Turn-around-time: The time taken from submission to receipt of the first peer review to eventual publication is an important criterion for selection. Journals can vary in their turn-around-times from a few weeks to up to one year or longer. This variation depends on the number of reviewers listed and available in the journal's data base, reviewer responsiveness and the rapidity with which the editor decides on acceptance, revision or rejection. Long turn-around-times are frustrating for authors as by the time their papers are published the findings may be out of date. The home page and author guidelines of a journal will usually state the average turn-around-times.

Readership access to journals: Before there was public access to the World Wide Web, the traditional form of publishing was through closed-access journals, usually in print form. Access to the articles in these journals was available through subscriptions or individual article fees which were expensive. In contrast, open-access journals contain articles that are digital, online and free of charge for the reader allowing immediate and unrestricted access. However, open-access literature is not free as management and processing costs are incurred. These costs are paid upfront either by the authors or a sponsor on acceptance of an article for publication. Many formerly closed-access journals now function as "hybrids", either offering open access upon payment of a fee or offering delayed open-access after a period of 6-12 months. The high article fees, however, are a concern. These can vary from USD$1,000-5,000 per accepted article and most authors cannot afford these on their own. Solutions include: research budgets from governments and donors including a line item to cover publishing fees, pooled funding from multi-lateral donors, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and open-access journals offering waivers or subsidies for authors from low- and middle-income countries. (4)

Recommendations from experienced colleagues: A final criterion is a recommendation from a seasoned and experienced colleague who writes and publishes extensively. That colleague will be up to date about issues such as turn-around-time, ease of submission, quality of the final product and dissemination links provided by the journal.

Author guidelines: Once the journal is selected it is imperative that the author guidelines are downloaded and carefully read. Important information must be recorded and noted. This includes narrative word count limits, abstract word count limits, number of key words, short running titles, maximum number of tables/ figures, maximum number of references, reference styles and other necessary back matter. Authors must adhere to these instructions.

12.3   What are the key elements of an operational research article?

The key elements are included in the acronym "IMRAD"- Introduction, Methods, Results, Discussion (Conclusion). These form the so-called "meat" of the manuscript to which are added other important components, such as the front matter (title page, abstract, key words) and back matter (acknowledgements, author contributions, funding statements, institutional review board statement, conflicts of interest and disclaimers).

The bulk of OR is observational with studies mainly using quantitative data. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement published in 2007 provides guidelines and a checklist for how to write a complete, accurate and methodologically sound report of an observational study. The STROBE statement provides a checklist of 22 items that relate to the title, abstract, introduction, methods, results and discussion sections of the articles and these are shown in brief format in Table 12.3. Two additional items should be included that do not appear in the STROBE check list: i) local relevance of the research question (i.e., does the study have operational implications and the potential to influence policy and practice?); and ii) the presence of an ethics statement.

Table 12.3 Simplified version of the STROBE statement recommendations (5)

Component	Item	Recommendation
Title / abstract		
	1	Provide a balanced summary in abstract of what was done and what was found. Indicate study design in title or abstract.
Introduction		
Background	2	Explain scientific background and rationale for the study
Aim / objectives	3	State aim and objectives in the last paragraph
Methods		
Study design	4	Present key design elements – cohort, case-control, cross-sectional
Setting	5	Present general and local setting and explain programme details
Participants	6	Present study participants (cases and controls) and recruitment period
Variables	7	List exposure and outcome variables
Data sources	8	Provide sources of data and methods of assessment
Bias	9	Describe any efforts to address potential sources of bias
Sample size	10	Explain how the sample / study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analysis
Statistical analysis	12	Describe all statistical methods, comparison analyses, missing data
Results		
Participants	13	Describe numbers at each stage of the study, consider flow diagram
Descriptive data	14	Describe characteristics of participants (demographic, social, clinical)
Outcome data	15	Report outcome events
Main results	16	Give unadjusted estimates, their precision and confounders adjusted for
Other analyses	17	Report other analyses done – e.g., sub-group analyses
Discussion		
Key Results	18	Summarise key results in relation to study objectives
Limitations	19	Discuss limitations of the study and potential bias or imprecision
Interpretation	20	Give overall cautious interpretation of results
Generalisability	21	Discuss generalisability (external validity) of study results
Other information		
Funding	22	Provide sources of funding and role of funders in the study

OR may also use qualitative data or both quantitative and qualitative data (mixed-methods). The COREQ checklist (not shown) provides guidelines and a 32-item check list to promote explicit and comprehensive reporting of qualitative studies (interviews and focus groups). (6)

12.2.1 How to develop an inspiring title?

Titles need to give specific information about the study. It is good practice to include the study design if the title character count allows (although the STROBE statement specifies that this can be given instead in the Abstract). "Who, where and when" is a simple aide memoir for remembering what to include in the title. The format can vary from a straight one-part statement to a two-part statement to a question. Some journals specify a set number of characters for the title which includes spaces between words and this can constrain what is written. Public Health Action, for example, specifies a title of no more than 110 characters.

The best way of developing an inspiring title is for the authors to bring ideas to the table, focusing on what the study is about and reviewing titles on PubMed from previous research studies in the same field. Some examples of operational research titles used in previous published and well cited research articles are shown in Table 12.4.

Table 12.4 Examples of research titles

No sex please – we're on TB treatment
The HIV-associated tuberculosis epidemic – when will we act?
The published research paper: is it an important indicator of successful operational research at the programmatic level?
Mortality reduction associated with HIV/AIDS care and antiretroviral treatment in rural Malawi: evidence from registers, coffin sales and funerals
Hand hygiene compliance at two tertiary hospitals in Freetown, Sierra Leone, in 2021: a cross-sectional study

12.2.2 How to write the Introduction section?

The Introduction sets the scene and concludes in the last paragraph with the specific question to be addressed in the form of the study aim and objectives. A well-used format is to start "global" and move to "local". Thus, in the first one or two paragraphs the authors can present the subject area in global terms along with the knowledge gaps. In the next one or two paragraphs they can present the subject area in the country where the work is being done along with the country-specific gaps. The authors should briefly present what has been done before in the study area with bibliographic citations but must avoid a long comprehensive review of the literature. The authors conclude by outlining the rationale for conducting the study and follow this by the study aim and objectives. The study aim is essentially the research question and it should be broad enough to encompass all of the specific objectives. The authors should have no more than three or four specific objectives under a broad study aim. The protocol, if well written, will form the basis of this Introduction.

12.2.3 How to write the Methods section?

The Methods section should follow the STROBE guidelines with the sub-headings shown in chronological order as shown in Table 12.5. Again, the protocol, if well written, will form the basis of the Methods section.

Table 12.5 Methods

Method sub-section	Comment
Study design	State whether it is cohort, case-control or cross-sectional study, mention whether data are secondary (already collected) or primary (to be collected)
Setting	Explain general setting (country, district) and site-specific setting. Mention how the programme functions and how data are routinely monitored and recorded
Study population	Mention any inclusion / exclusion criteria, include sample size calculation if appropriate, and state recruitment period
Data variables	List variables in relation to the study objectives

Sources of data	List sources of data for each variable and how data are collected
Analysis and statistics	Outline analysis plan, statistical tests to be used, use of 95% confidence intervals and levels of significance (usually set at 5% - P<0.05)
Ethics considerations	Usually enough to state the study permissions and ethical approvals but other issues could be presented if deemed applicable. These might include comments on data confidentiality, benefits and risks for participants and community

12.2.4 How to write the Results section?

The narrative part of the Results section reports the facts and nothing but the facts. The facts should be presented in relation to the study objectives and should follow these in chronological order. The key facts are the response rate, the demographic and clinical characteristics of the study population, the outcomes and factors associated with specific outcomes. Most of the numeric results will be presented in tables and figures and authors must avoid duplication in the narrative text and tables. The narrative must draw attention to the key facts of interest without discussing every variable shown in the tables and figures. With the statistics the authors should focus on planned outcomes and avoid the temptation to compare everything with everything.

12.2.5 How to prepare Tables and Figures?

Tables and Figures must stand alone, i.e., meaning that the Table / Figure title and legend must fully explain the "Who, What, Where and When" of the data being presented without need to refer to the Results narrative. Tables and Figures must be understandable without the text of the paper.

Authors should prepare tables using the "insert table" function of word. The number of columns and rows need to be worked out in advance. Once decided upon, all borders (outside and inside for columns and rows) should be retained until the table is ready for submission. To ensure that numbers and percentages of a particular variable are neatly placed next to each other, the numbers in the column should be right aligned and the percentages in the adjacent column should be left aligned. It is recommended to use no more than one decimal place. All abbreviations used in the Table should be explained in the footnotes. When ready for submission, all column borders should be removed and the only row borders that should remain are the top and bottom as well as the internal border under the column titles. The anatomy of a table in a submitted manuscript is shown in an example in Figure 12.1.

Figure 12.1 Anatomy of a table

Authors should prepare Figures in Excel, EpiData, Stata, SPSS and so on. The same principles apply as with preparing a table. The anatomy of a figure in a submitted manuscript is shown in an example in Figure 12.2.

Figure 12.2 Anatomy of a figure
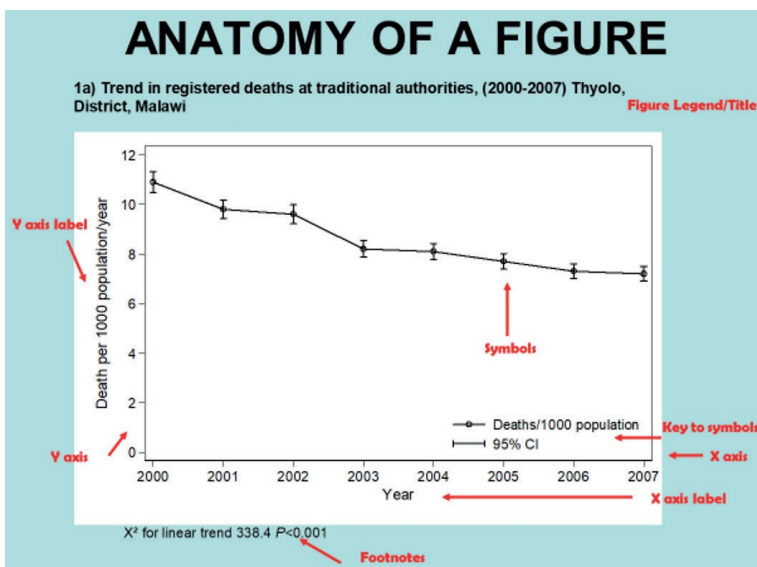
Tables and Figures must be numbered consecutively as they appear in the text. Journals vary as to how they want them presented. This can be either within the Results narrative right after the narrative text, e.g., "See characteristics of the study population in Table 1" or at the end of the manuscript with Tables and then Figures listed chronologically on separate pages. Journals often specify a maximum number of Tables and/or Figures. Sometimes a journal allows only a small number of stipulated Tables/ Figures. This can be circumvented by labelling Figure 1 as Figure 1A, Figure 1B and Figure 1C! Remember to read the author guidelines carefully.

12.2.6 How to write the Discussion and Conclusion section?

This part of the manuscript is the most interesting and yet the most difficult to write. A schematic outline of how to structure this is shown in Table 12.6.

Table 12.6 Discussion and Conclusion

•   Brief summary of findings and what is new, focus on two or three key findings
•   For each key finding: first, second and third: in narrative form: explain the finding, show how the finding compares with findings of previous studies and outline possible reasons for the findings
•   Strengths and limitations of the study
•   Implications and recommendations of the study
•   Conclusion (some journals request a separate conclusion section)

Useful tips for consideration include the following:

- Avoid repeating the facts in the Discussion – they have already been presented in the Results and Tables/Figures.

- Some journals request that strengths and limitations are placed at the end of the manuscript, just before the conclusion. A justification of placing strengths and limitations before the implications and recommendations is that it gives readers a sense of how methodologically strong the study is and enables them to trust (or not) the implications and recommendations of the study.

- Strengths would include, e.g., country-wide coverage, large sample size, robust methodology, attempts to minimise bias, reporting of the study in line with STROBE or COREQ guidelines.

- Limitations could include, e.g., missing data, variables not included in the database but which would have been useful to explain the study finding.

- A conclusion paragraph or section (depending on the author guidelines) should be kept short and simple and used to briefly summarise the main study findings, the implications and recommendations related to the initial aim and objectives.

12.2.7 How to write an abstract?

Authors should always write the abstract after the full paper is completed. Given that the abstract is what most people only read, time and effort should be devoted to ensuring that this section is as good as possible. Journals specify the number of words allowed in an abstract and this can vary from 200 to 350 with short research articles often allowing just 100 words. Journals also specify whether their abstracts are structured or unstructured. A structured abstract has sub-headings: Public Health Action, for example, requests five sub-headings and these are included in the 200-word count limit: Setting, Objective, Design, Results and Conclusion. An unstructured abstract has no sub-headings and is a single paragraph in which the authors must provide relevant background and context as to why the study has been done, the aim and objectives, brief methodology, including the study design, the key results and conclusions.

12.2.8 How to select keywords and how to write a short running title?

Key words: Most journals require authors to select key words for their articles, the number varying from three up to ten or more. Key words are those that help the article to be identified when researchers are searching PubMed or other search engines for relevant articles. In selecting key words, authors should follow the publisher's guidelines, focus on terms related to the main topic of the research and avoid duplicating words that have been used in the title. Authors should be specific and use multi-word "key phrases" wherever possible: for example, "tuberculosis treatment success rates" would be one key word. Once authors have selected some key words, they can try them out by entering them into a relevant journal database or PubMed and see whether they bring up articles on similar topics. Alternatively, if authors are struggling to come up with key words that work, they can search for some articles that cover the same subject, check their key words and use these to guide their choices.

Short running titles: Many journals request short running titles that vary in length from 40 – 100 characters that include spaces. This shortened form of the main title is usually cited at the top of each published page of an article and serves to guide readers browsing a print journal, shuffling loose printed pages or toggling between multiple papers in PDF form.

12.2.9 What are the other bits and pieces that are important to complete a manuscript?

Journals often categorise these "bits and pieces" into front matter and back matter.

Front matter includes title page, abstract and key words. The title page contains the manuscript title, the names of the authors, their affiliations and information about who is the corresponding author. An example of how this might appear is taken from reference [7] and shown in Table 12.7.

Table 12.7 Front matter

Title: Fast-track writing of a scientific paper with 30 authors: how to do it
Authors: S. Satyanarayana[1,2], A.M.V. Kumar[1,2], B.N. Sharath[3], A.D. Harries[1,4]

Affiliations:
  1. South-East Asia Office, International Union Against Tuberculosis and Lung Disease, New Delhi, India
  2. Centre for Operational Research, International Union Against Tuberculosis and Lung Disease, Paris, France
  3. Central Tuberculosis Division, Ministry of Health and Family Welfare, New Delhi, India
  4. London School of Hygiene and Tropical Medicine, London, UK

Corresponding author: Srinath Satyanarayana, address, phone number, email

Back matter varies from journal to journal and common components are shown in Table 12.8.

Table 12.8 Back matter

Back matter	Comment
Author contributions	Journals often provide a template for author contributions to be completed that might include study conception, methodology, data collection, formal analysis, writing the first draft, reviewing and editing. Authors can tick those components that they contributed to
Funding	A statement about who funded the study and the role (if any) of the funders
Ethics statement	Ethics statements may be included in Methods or in the Back matter
Informed Consent	Informed consent statement if this was used in the study
Data availability ★	Statement about how data can be made available to the readers. Data can be deposited into software, such as "Figshare"
Acknowledgements	Acknowledging persons who assisted with the study and who are not listed as co-authors
Conflicts of Interest	If none, then include a statement stating "authors declare no conflicts of interest"
Disclaimer	If applicable, for example, it could read "The views expressed in the paper are those of the authors and do not necessarily reflect those of their institutions"

12.2.10 What about writing style?

Every person's writing style is unique. However, there are a few tips to help with the writing of a scientific paper as shown in Table 12.9.

Table 12.9 Writing style

Tips	Comment
Use simple and familiar words	
Avoid or minimise jargon	e.g., use "shortness of breath" rather than "dyspnoea"
Keep sentences simple	Aim for 15-20 words
Keep paragraphs short	Aim for 5- 6 sentences
Avoid unnecessary words	e.g., "It is the case that….."; "It is known that….."
Use active voice rather than passive voice	e.g., "the study team administered the questionnaire"
Avoid emphasis words	e.g., "really"; "very";
Check the use of tense	Past tense versus present tense
Check spelling and grammar	Use Word Tools for spelling and grammar
Do not start a sentence with a number	e.g., "Fifty persons completed therapy"

12.3   How to handle author collaboration?

The inclusion of authors and the order of authorship are important issues to consider in the writing of a scientific paper. They should be discussed early when developing the research study. Preferably all the authors should be included and listed in chronological order in the research protocol. The most recent criteria (2014) for being an author according to the International Committee of Medical Journal Editors (ICMJE) (available at www.icmje.org/.../defining-the-role-of-authors-and-contributors. html) are shown below.

*Data availability: many journals request that data be made available to readers. There are several ways of doing this. A simple way is to say that "data are available upon request of the principal investigator" and provide contact details. Another way is to deposit data into established software, such as "Figshare". This is an online open access repository where researchers can preserve and share their research outputs, including tables, figures and datasets. It is free to upload content and free to access, in adherence to the principles of open data sharing. More information about registration and use of "Figshare" can be found at https://figshare.com.

Table 12.10 Criteria for authorship

• Substantial contributions to the conception or design of the article or the acquisition or analysis or interpretation of data for the work; AND
• Drafting the article **or** revising it critically for important intellectual content; AND
• Giving approval for the final version to be published; AND
• Agreeing to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All those designated as authors should meet all four criteria for authorship and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria but have nevertheless made contributions to the work should be acknowledged.

OR is not only about publishing a paper. It is about collecting, analysing and interpreting solid evidence that may help in getting policy and practice changed so that health delivery is improved. In this regard, the authorship should include programme managers and decision makers who can be involved in development of the research question and who can make important contributions to implications and recommendations that arise from the study.

The three most important authors are the first author, the senior author and the second author.

The **first author** does most of the work in implementing the project and in getting the manuscript ready for submission. This person is usually the corresponding author and takes the lead in submission of the paper to the journal, manages the responses to the journal editor and peer reviewers and deals with the author declarations and signatures that are required after acceptance of the paper for publication. The first author will tick most of the check-list boxes that are provided by journals for author contributions.

The **senior author** is usually placed last in the list of authors. He/she takes responsibility for the framework of the study and manuscript and makes the important final decisions about the most appropriate journal, the various drafts of the paper, the readiness for submission and assisting and signing off with responses to reviewers. This position is also seen as one of respect for a senior author who may in fact not have had such an active role in the development of the article.

The **second author** is generally the person who makes the next largest contribution to the article after the first and senior author. Other co-authors undertake tasks as requested by the first and senior authors, such as drafting specific sections of the manuscript in their particular area of expertise and will fulfil the criteria for being an author as shown above.

Before submission it is important to get all authors to write and state that they have read the final version of the manuscript and approve it for publication. If a co-author fails to do this, the first and senior author may have no option but to remove that person from the manuscript.

12.4 How to prepare the final manuscript and handle the journal submission process?

Details of the final manuscript must be checked against the author guidelines to ensure that word counts, number of tables and figures, references and reference styles are adhered to. Journals will specify how they want tables and figures to be submitted, either embedded within the paper, presented at the end of the paper or submitted separately.

Most journals request a cover letter. This is addressed to the Editor and explains in no more than one page what the study is about, why it is important and why this particular journal has been chosen. It is good to conclude the cover letter by saying that all authors have read and approved the final manuscript and the manuscript has not been submitted anywhere else for consideration of publication.

All journals now require an electronic submission. The first (corresponding) author should follow the author guidelines and assemble all the pieces beforehand.

It is important to have the names, affiliations and email addresses of all co-authors as these will be needed in the submission. Many journals also request the name, position, institutional address and email address of three or more reviewers that the authors recommend though these reviewers are not always used. Sometimes, journals ask for the names of up to three reviewers whom the authors do not want to be invited to review the paper.

The first (corresponding) author does the submission. He/she will need to register with the journal before proceeding and set up a unique username and password. Then it is a simple matter of following the instructions and completing the pages and the boxes one by one. The final version of the manuscript should be open on the computer and the submitting author can copy and paste various sections of the manuscript into the appropriate boxes (e.g., title, abstract, key words). The process in many journals follows a format that is similar to what is shown in Table 12.11.

Table 12.11 Process of submitting a manuscript to a journal

• Select from a pull-down menu the type of article being submitted, usually "an original article"
• Enter title, abstract, short running title and key words in the appropriate boxes. Pay attention to word count or character count limits
• Upload the full manuscript with tables/figures and the cover letter
• Enter names, affiliations, email addresses of all the authors in chronological order
• Enter names, affiliations, email addresses of three or more potential reviewers
• Complete other bits and pieces, such as narrative word count, number of tables/ figures, funding statement and for open-access journals to whom the invoice should be sent if the article is accepted
• Final page: check that the submission is accurate and that the PDF and HTML versions of the manuscript are correct
• Press SUBMIT

If the manuscript has been successfully submitted, the corresponding author (and sometimes all authors) will receive a notification email from the journal.

12.5 What happens to the submitted manuscript and how should reviewer comments be addressed?

The manuscript will be assigned to an editor who will decide whether the manuscript will proceed for peer review. If suitable, the manuscript is sent to peer reviewers (frequently between two and four) and they will be asked to provide feedback to the editor within two to three months. The editor reviews the feedback, decides whether the manuscript will be accepted, revised or rejected and returns this decision and the reviews to the corresponding author. It is essential that the authors read the editor's letter carefully. Samuel Johnson, the great 18th century English writer, once said of a manuscript he had reviewed "Your manuscript is at once good and original. However, the part which is good is not original and the part that is original is not good". There are four possible editorial decisions as shown below.

Table 12.12 The four possible editorial decisions on a manuscript

Accept	A rare occurrence which happens in less than 5% of submissions. This decision demands immediate celebration
Accept after revision / minor revision	Small revisions requested and the manuscript will be accepted if these revisions are attended to
Revise / major revision	Large revisions are needed and there is no guarantee that the revised manuscript will be accepted and further reviews should be anticipated
Reject	This decision is usually accompanied by the reviewer comments. Authors should consider appealing or submit the manuscript to another journal

On receipt of the editor's letter the corresponding author should copy and paste all the comments from the editor and reviewers into a blank Word document. The task ahead is now to address all these comments with "point-by-point responses" and where requests are made to revise the paper to proceed accordingly.

Every point brought up by the editor and reviewers must be addressed politely. An overview statement thanking the editor and reviewers should accompany these point-by-point responses because they have spent unpaid time and effort giving their guidance on how to improve the manuscript. If the authors disagree with the reviewer's recommendations, a justification needs to be made. An example of how to write a point-by-point response is shown in Table 12.13.

Table 12.13 Example of points-by-point responses

Lancet Infectious Diseases: Diagnosis and management of antiretroviral therapy failure in resource-limited settings in sub-Saharan Africa: challenges and perspectives D-09-0630 [8]

To the Senior Editor Lancet Infectious Diseases

Dear Editor,

Thank you very much for the comments of the reviewers and the editor. We have attempted to address all these comments and give a point-by-point response below. We copy the comments below and respond using **bold font**.

Reviewer #1:

We thank the reviewer for the useful and relevant comments and we provide point-by-point responses

1. Introduction: paragraph 2, line 2 - you mean that 97% of adults and children who were on treatment remained on first line regimens, not 97% overall.
   Response: Yes, and we have revised this sentence accordingly.

2. Introduction: you should also reference abstract MOAB104 from the IeDEA study in South Africa presented at Cape Town this year where 11% of children on antiretroviral therapy at 3 years were failing and 50% were not switched to second line therapy and those who were switched had significant delays.
   Response: We have modified the Introduction and we have included a sentence on the IeDEA study and added a relevant reference to support this.

3. In the introduction you should separately discuss the implications of failing because of lack of access to drugs and failing because of poor adherence as they have quite different implications.

   Response: We have modified this paragraph and included reasons for resurgence or persistence of HIV in the blood that include drug stocks outs, poor adherence due to side effects or other factors, use of standard first line ART following single dose nevirapine to prevent perinatal HIV transmission and inadequate nevirapine levels as a result of concomitant use of rifampicin in HIV-infected tuberculosis patients. We believe from our Malawian experience that lack of access to drugs leads to poor adherence because patients take half doses or share with relatives or friends but we recognise the journal's word limits and have not got involved in a discussion of these finer details.

4. In the introduction given your comparison to the UK you might also cite some figures on failure rates in those countries or in clinical trials conducted in those countries for comparison.

   Response: We wondered how relevant it is to include data from UK or Europe as the management of ART is so different in these countries. We again recognise the journal's word limits and have also added a number of references to address other points (see below). As a result, we have not amended this section.

5. One other reason for virologic failure is giving single dose Nevirapine for mother to child transmission.

   Response: Thank you, this is a good point. We have included this and added two references.

The manuscript must be revised in line with these responses. Journals provide instructions on how to do this using tracking changes, a different colour font or highlighting the changed text.

12.6 What are the other steps needed between acceptance and publication of the manuscript?

Once the manuscript is accepted, there are a number of tasks that may need to be done before the paper is published and these are outlined below.

Table 12.14 Common tasks required before an accepted manuscript is published

Outstanding queries	There may be further editorial queries that need to be addressed
Signed author statements	These vary according to the journal
Signed conflicts of interest forms	Signed conflicts of interest declaration forms vary in format
Settling the invoice to be paid	Open-access fees to be paid
Proofs and queries	Proofs to be carefully read and queries to be addressed
Data set to be shared	Consider using the "Figshare" repository
Beyond the publication	Consider how to move the findings to policy and practice.

References:

1. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; 374: 86-89.

2. Zachariah R, Tayler-Smith K, Ngamvithayapong-Yanai J, et al. The published research paper: is it an important indicator of successful operational research at programme level? Trop Med Int Health 2010; 15: 1274-1277.

3. Rujumba J, Byamugisha R. Publishing operational research from "real life" programme data: a better form of accountability. Trop Med Int Health 2012; 17: 133-134.

4. Zachariah R, Kumar AMV, Reid AJ, et al. Open access for operational research publications from low- and middle-income countries: who pays? Public Health Action 2014; 4: 141-144.

5. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007; 370: 1453-1457.

6. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007; 19: 349-357.

7. Satyanarayana S, Kumar AMV, Sharath BN, Harries AD. Fast-track writing of a scientific paper with 30 authors: how to do it. Public Health Action 2012; 2: 186-187.

8. Harries AD, Zachariah R, van Oosterhout JJ, et al. Diagnosis and management of antiretroviral therapy failure in resource-limited settings in sub-Saharan Africa: challenges and perspectives. Lancet Infect Dis 2010; 10: 60-65.

13 Communicating operational research findings through engagement with stakeholders

This chapter discusses how to develop an actionable message, how to identify the right audience for dissemination, selecting who should deliver the message, the best tools for delivering the message and the platforms that can be used for dissemination.

13.1 How to develop an actionable message?

The first step in developing an actionable message is to complete the write up and submission of the scientific article to a peer reviewed journal. This allows the research to be placed in the context of previously published research on the same subject and the key finding(s), implications and recommendations of the research study to be clearly presented and articulated. These then need to be translated into key messages. It is good practice to have no more than three key messages. These should be prioritised by order of importance and, if possible, presented as one actionable message. The message or messages to be disseminated depend on the study findings and the possible policy or practice change(s) that are anticipated. These changes may be at the local health facility or laboratory level or at the national or even international level. The message itself may change depending on whom it is mostly directed to – for example, a scientific audience, local, national or international decision and policy makers or the general public. Figure 13.1 shows the important differences between the process of conveying information to a scientific audience and the process of conveying information to a wider and more general audience.

Figure 13.1 Communicating an actionable message

Developing a key actionable message is not an easy task and researchers should work closely with communications and advocacy teams, if available, to support this work.

Example: The SAPIT (Starting antiretroviral therapy [ART] in three points in tuberculosis therapy) trial in South Africa provides a good example of how messages should be developed to the audience. The trial investigated the optimal time to initiate antiretroviral therapy during tuberculosis treatment. (1) Table 13.1 shows the concluding headline scientific message of the research study directed at scientists and policy makers in the New England Journal of Medicine and the simple headline that was subsequently published in the New York Times directed at the general public.

Table 13.1 Conveying research messages to difference target audiences

New England Journal of Medicine	Target audience: scientists and policy makers Conclusion: The initiation of antiretroviral therapy during tuberculosis therapy significantly improved survival and provides further impetus for the integration of tuberculosis and HIV services
The New York Times	Target audience: general public Headline: Treating tuberculosis and AIDS together saves lives

13.2 How to identify the right audience for dissemination?

Once the article is finalised and submitted for publication, thought must be given to identifying and mapping the target audience for dissemination. This will include colleagues, programme managers, local, national, regional and international policy makers, healthcare workers, patients, the media and the general public. It is helpful to generate a list of all potential stakeholders and through this list identify those who can help and work for you. Who might hinder and work against you? What level of power or influence does each stakeholder have? And how would each stakeholder best like to receive the information?

Conceptualising who are the key influencers, the key players and the key interest groups as shown in Table 13.2 is a good start.

Table 13.2 Deciding on the right target audience*

KEY INFLUENCERS	KEY PLAYERS
Journalists Social media Financiers	Programme managers Decision makers Policy makers
NON-KEY PLAYERS	**KEY INTEREST GROUPS**
General public	Patient groups

*Adapted from SORT IT Course, Module 4

The next step is to develop a stakeholder template as shown in Table 13.3. Once developed, the research team needs to compile a list of stakeholders, position them row by row within the matrix and place those of most importance to getting policy or practice changed in the top rows.

For each stakeholder, the following information should be recorded: the name, contact details, how the findings will impact the stakeholder and how powerful and influential they might be in effecting change. There must be an honest appraisal of how the stakeholder might contribute both positively and negatively towards the dissemination and implementation of recommendations. Finally, it is helpful to document how contact with the stakeholder will be made and what type of engagement strategy will be used.

Table 13.3 Example of stakeholder map*

Stakeholder map							
Stakeholder name	Contact details	Impact[1]	Influence /Power[2]	Importance to stakeholder[3]	Positive contribution[4]	Negative contribution[5]	Engagement strategies[6]

13.3 Who should deliver the message?

It is important to reflect on who can best bridge the gap between the producers of the knowledge (the researchers) and the users of this knowledge. These so called "messengers" may vary depending on how and where the message is being delivered.

*Adapted from SORT IT Course, Module 4

[1] The impact that the findings may have on the stakeholder (low, medium or high)
[2] How much influence / power the stakeholder has over policy change (low, medium or high)
[3] What is the importance of the research findings to the stakeholder
[4] How can the stakeholder contribute to dissemination and implementation of recommendations
[5] How might the stakeholder hinder dissemination and implementation of recommendations
[6] What are the strategies for engagement: one-to-one meeting; group meeting; formal presentation

It is important to decide who can best bridge the gap between the producers of the knowledge (the researchers) and the users of this knowledge. These so called "messengers" may vary depending on how and where the message is being delivered.

For example, the key people to deliver the message to a scientific audience at a meeting or a conference will be the first author and the senior author of the study. As explained earlier, they will have done most of the work in conducting the study and bringing it to its conclusion. They will also be the most knowledgeable about how the research findings fit within the current literature, what are the implications and the key recommendations of the study. They may also be the best people to deliver the message at a press conference to the media, the general public and other interested stakeholders, although bringing in a communication expert can help in bringing clarity to the presentation.

Knowledge brokers or policy entrepreneurs may be used to explain the meaning and practical implications of the findings to decision makers in Ministries of Health. (2,3) These people work within the programme management team and are usually well trusted by decision makers in the ministries. Their role would include raising awareness of the decision makers to the important findings and bringing stakeholders together to begin the decision-making process.

13.4 What are the best tools for delivering the message?

The key tools for this task are the plain language summary, power-point presentations and an elevator pitch.

Plain language summary: This should be a short concise summary (handout) of the article in plain language that a non-expert can read and understand. Preferably, it should not be longer than two pages. The summary includes the implications of the study findings and suggests changes that might be made to improve the situation. The recommended structure is shown in Table 13.4. It is best to use active rather than passive language, short paragraphs, font size 12 and emphasise important points in bold or italic font.

Table 13.4 Structure of a plain language summary★

Headings	Comments
Title	Concise, brief and informative
Key messages	Up to three key messages in bullet point form <200 words
What is the problem and why is it important?	The context < 150 words
How did we measure it?	Methodology < 150 words
What did we find?	Results- no more than three bullet points <150 words
What are the implications / Recommendations	Consequences and solutions <200 words

★Adapted from SORT IT Course, Module 4

Power point presentations: Two types of power point presentations (PPPT) can be prepared. A 10-minute PPPT designed for a scientific conference and a 3-minute (lightening) PPPT designed for policy and decision makers or the general public. How to prepare PPPT is beyond the scope of this guide but there are a few useful tips to impart.

• PPPT allows visual presentation of data. This can be done in several ways: histogram, scatter plot, line graph, stacked area graph, bar/column graph, stacked bar graph and pie chart. Keep the data simple, use the same colours and avoid 3D effects.

• Feel free to use images under the Creative Commons License.

• Keep the font size legible, e.g., 24-28 font.

• Keep the slides neat and tidy and limit the amount of information on each slide.

A 10-minute PPPT would follow the IMRAD structure with title, background, aim and objectives, methodology, research results, implications, key recommendations and conclusion.

A 3-minute (lightening) PPPT should be different. After the title, this type of PPPT could start with a strong headline slide followed by background slide (that includes methods), results (1 or 2 slides), a slide showing the link between evidence, implications and recommendations (Figure 13.2) and a final take away message slide (Figure 13.3). The PPPT slide shown in Figure 13.3 is from an OR study on hand hygiene compliance amongst healthcare workers in two tertiary hospitals in Sierra Leone. (4)

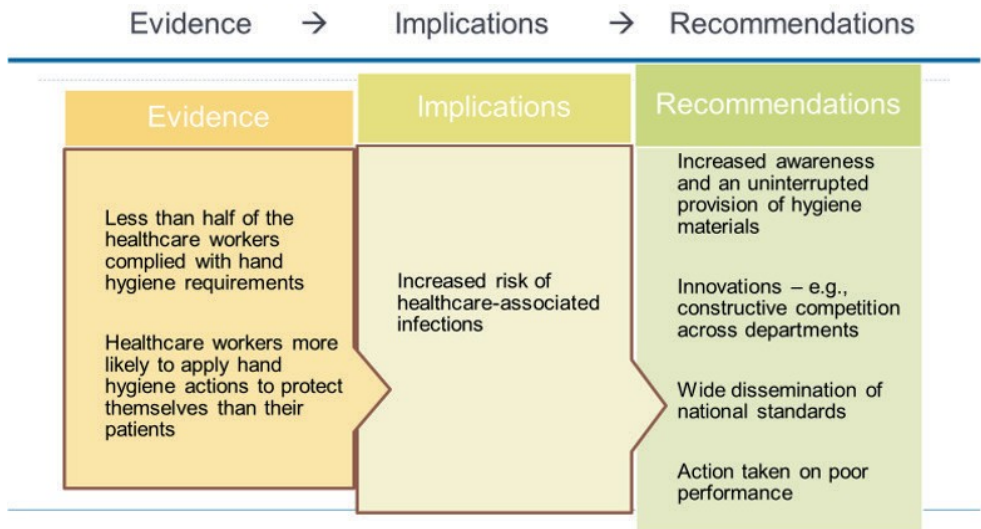**Figure 13.2** Linking evidence to implications to recommendations

Figure 13.3 The takeaway message

Elevator pitch: This is a short oral presentation of approximately 30-60 seconds delivered to a decision maker in a hotel elevator in the hope that the decision maker will be interested enough to allow further discussion on the subject, either at a one-to-one meeting or at a more formal and larger meeting.

Example: This is an elevator pitch that followed a hand hygiene compliance study in Sierra Leone.

- Hello, I am Lt. Gladys Kamara working for the Sierra Leone Armed Forces. I have just completed an observational study on hand hygiene compliance amongst health care workers at two tertiary hospitals in Freetown.

- I found that in over 10,000 hand hygiene opportunities observed less than half of the healthcare workers practiced hand hygiene appropriately. Furthermore, healthcare workers were more likely to apply hand hygiene actions to protect themselves rather than to protect their patients.

- There are several things we can do in Sierra Leone to improve on this. Can I send you my hand-out or set up a meeting with you for a short presentation and discussion?

13.5 Which platforms may be used for engaging with stakeholders?

A variety of different platforms can be used to disseminate the message(s) and engage with stakeholders. These can vary as follows: one-to-one informal meetings or larger more formal meetings with decision makers, formal presentations at scientific conferences either at local, national or international level, press conferences with journalists and other interested stakeholders, engagement with traditional media, such as newspapers, radio or television and finally, engagement with social media platforms through Face book, Twitter, Instagram, etc. Whatever platform is used, the speaker needs to be prepared thoroughly, honing concise messages about what the research has found, what it means and what should be done and preparing answers for likely questions.

References:

1. Abdool Karim SS, Naidoo K, Grobler A, et al. Timing of initiation of antiretroviral drugs during tuberculosis therapy. N Engl J Med 2010; 362: 697-706.

2. Sin CH. The role of intermediaries in getting evidence to policy and practice: some useful lessons from examining consultancy-client relationships. Evidence & Policy 2008; 4: 85-103.

3. Zachariah R, Ford N, Maher D, et al. Is operational research delivering the goods? The journey to success in low-income countries. Lancet Infect Dis 2012; 12: 415-421.

4. Kamara GN, Sevalie S, Molleh B, et al. Hand hygiene compliance at two tertiary hospitals in Freetown, Sierra Leone, in 2021: a cross-sectional study. Int J Environ Res Pub Health 2022; 19: 2978.

14   Evaluating the impact of operational research

This chapter discusses the importance of impact evaluation of an OR study, a framework that can be used to assess and evaluate impact of an OR study and how this evaluation can be carried out.

14.1   Why is impact evaluation of OR important?

The goal of OR is to enhance the quality or coverage of disease control programmes, health services or health systems. The publication of a research paper in itself is not enough. What is wanted is change for the better in policy and/or practice which should lead to better programme performance and ultimately improved health outcomes. It follows we need impact evaluation of OR projects. An example of the importance of impact evaluation is illustrated through a case study from Malawi (Table 14.1).

Table 14.1 A case study from Malawi illustrating the importance of impact evaluation in operational research

The advent of HIV in Malawi severely affected the National Tuberculosis Programme (NTP) with tuberculosis case fatality rising from 5% in the pre-HIV era to above 30% during the height of the HIV epidemic. A randomised controlled trial in Cote d'Ivoire, from 1995-1998, showed that adjunctive cotrimoxazole administered to HIV- positive people with tuberculosis almost halved the mortality rate [1]. Based on this evidence, the Ministry of Health in Malawi asked the NTP to assess whether a package of voluntary counselling, HIV testing and adjunctive cotrimoxazole (for those found HIV-positive) might reduce the high mortality in people with tuberculosis routinely registered for treatment.

An OR study was conducted in one of Malawi's Southern Region districts between July 1999 and June 2000 [2]. In brief, all people with tuberculosis started on tuberculosis treatment were offered voluntary counselling and HIV testing. Those found to be HIV-positive were offered adjunctive cotrimoxazole provided there were no contraindications. These individuals were followed up in the usual way on a regular monthly and quarterly basis with close supervision. End-of treatment outcomes in this cohort (the intervention group) were compared with end-of-treatment outcomes in the cohort of people with tuberculosis registered the previous year between July 1998 and June 1999, in whom counselling, HIV testing and cotrimoxazole were not offered (the historical control group). Case fatality was the primary end-point and additional efforts were made to determine whether individuals in each cohort who were lost to follow-up or transferred out of the district during treatment had died during the treatment period.

Of the 1,061 people with tuberculosis in the intervention cohort, 91% were HIV tested, of whom 77% were HIV-positive, of whom 94% were given adjunctive cotrimoxazole. The case fatality rate in the intervention cohort was 28%, significantly lower than 36% in the historical control group. The study showed that it was feasible and safe for the NTP at the district level to implement the package of interventions and it was effective at reducing mortality. Another OR study with a slightly different methodology, conducted in the North of Malawi, produced almost identical results [3].

Once the studies had been completed, a Ministry of Health meeting was arranged in 2001 with many stakeholders to discuss the results and implications. This resulted in a policy of HIV testing and adjunctive cotrimoxazole being recommended for all people with tuberculosis in the country [4]. This policy was implemented and scaled up over several years and provided the framework for treating people living with HIV and tuberculosis with antiretroviral therapy once this treatment became available from 2004. The impact was huge. Death during tuberculosis treatment in people with smear-positive pulmonary tuberculosis decreased from 19% in 2002 to 7.5% in 2008. This was associated with a striking increase in treatment success, which rose from 72% to 86%.

14.2   Are there any frameworks which can be used to plan evaluation?

The theory of change is a useful framework for evaluating the outputs, outcomes and impact of research projects (Figure 14.1).

Figure 14.1 Theory of change
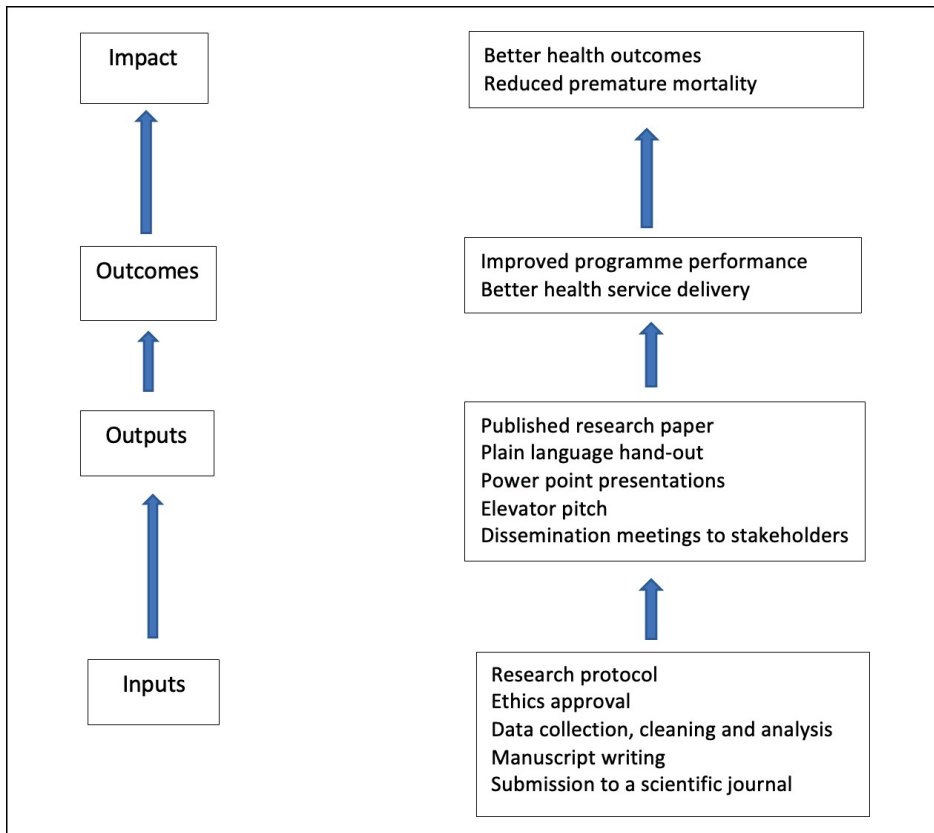
The inputs relate to all the important components of getting an OR project conceptualised and designed, funded and approved by ethics review boards. This is followed by collecting, cleaning and analysing data, writing the manuscript, submitting to a scientific journal, responding to editorial and peer review and finally getting acceptance for publication.

The outputs are the published paper in an open access journal, the tools for dissemination and the various dissemination meetings held with stakeholders to change policy and practice.

The outcomes can be sub-divided into short-term (1-3 years), medium-term (3-5 years) and long-term (5-10 years) with all of them relating to improved disease programme performance and better health service delivery. With respect to the Malawi case study presented above, the outcomes included counselling and HIV testing offered to all people with tuberculosis at the time of registration for tuberculosis treatment, provision of cotrimoxazole preventive therapy to those diagnosed HIV-positive, enhanced recording and reporting of HIV-related indicators that were included in the routine monitoring systems and generally, better follow-up of patients to the end of tuberculosis treatment which resulted in reduced numbers of patients lost to follow-up.

The impact is related to improved health outcomes and reduced premature mortality in the country where the project is implemented. It can take time to demonstrate impact as shown in Malawi (Table 14.2). (4) Case fatality during tuberculosis treatment only declined significantly when HIV testing was reached 50% and above of notified people with tuberculosis. This took almost five years.

Table 14.2 Relationship between outcomes and impact over time in Malawi

National tuberculosis case notifications, HIV testing and results and adjunctive cotrimoxazole (CPT)							
Year	2002	2003	2004	2005	2006	2007	2008
National tuberculosis case notifications	27,531	28,234	27,000	27,610	27,105	25,966	25,688
% HIV tested	8%	14%	25%	44%	64%	83%	84%
% of those tested HIV-positive	77%	69%	72%	69%	70%	72%	63%
% of HIV-positive given CPT	No data	86%	97%	96%	93%	89%	96%
Treatment outcomes in new smear-positive pulmonary TB patients evaluated nationally for outcomes							
New SM+ve PTB patients evaluated	7,693	7,603	8,021	7,965	7,955	8,065	7,632
% Treatment success	72%	74%	76%	78%	80%	83%	86%
% Death	19%	19%	17%	16%	13%	9%	7.5%
% Other outcomes	9%	7%	7%	6%	7%	8%	6.5%

SM+ve PTB = smear-positive pulmonary tuberculosis; Other outcomes = loss to follow-up, failure of treatment, transfer-out and not evaluated

14.3   How can impact evaluation be carried out?

The evaluation of impact of an OR project can be carried out in several ways depending on where the researcher is placed. If the researcher works within a national disease control programme, then a simple framework to monitor what is happening can be set up as shown below.

Figure 14.2 Framework for regular evaluation of operational research within a disease control programme

Research studies completed

Research papers submitted to scientific peer-reviewed journals

Research papers published

Research findings disseminated locally and nationally

Changes in policy and practice

Evaluation of effect on programme performance and health outcomes
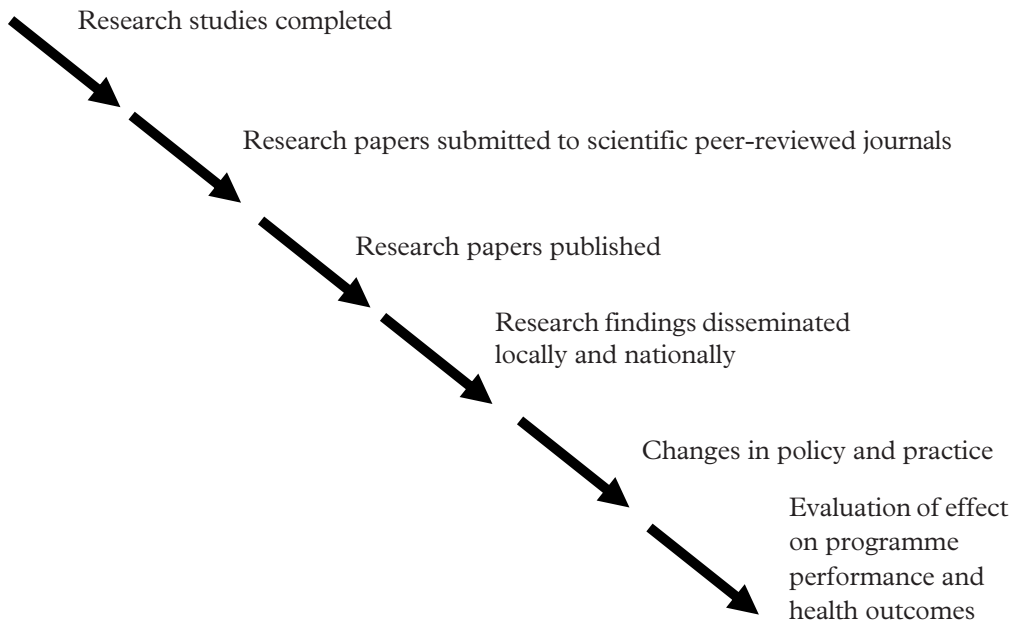
In Malawi, for example, between 1996 and 2004, a NTP management group was set up and it met every month to discuss programmatic issues and OR. The management group discussed and recorded in monthly minutes what research was needed for the programme, who would conduct it, the progress made with the research, decisions made about changes in policy and practice and information recorded about outcomes and impact (focused on programme performance and patient treatment outcomes). There was an annual OR report which followed the standardised framework shown above.

If the unit that coordinates and monitors the research is outside of the disease control programmes or outside the country in which the research has taken place, questionnaires will need to be sent to implementing researchers to enquire about policy and practice change. For example, The Union has been organising and running Structured Operational Research and Training Initiative (SORT IT) Courses since 2009, in which participants from countries around the world develop and implement research projects and bring these to a conclusion with the submission and publication of a paper in a scientific journal. (7)

It has been standard practice to follow-up SORT IT alumni 18-months after completion of the course to establish whether there has been any change in policy and/or practice as a result of the research. The methodology involves sending to each course participant a self-administered questionnaire through email or web-survey and following up with telephone/Skype/in-person responses. The key question asked is simple: "Has the research study you undertook and the paper you published had an effect on policy and practice? If YES, please state the effects on policy and practice; if NO, please provide possible reasons".

There have been three separate evaluations to date, which have been published. (8,9,10) In total, 234 participants had their published research papers evaluated, of which 153 (65%) self-reported that their research study had an effect on policy and practice. The changes reported occurred in the Ministry of Health at national, subnational and local hospital level and also within non-governmental organisations, such as Médecins Sans Frontières (MSF). The types of change included redrafting of national guidelines, scaling up of existing policies, modifications of monitoring and evaluation tools, and improving programme implementation and practice. Reasons for lack of policy and/or practice change included lack of priority of the research question to policy makers, need for more time to effect change, ineffective dissemination of the findings and high turn-over of decision makers in key positions in Ministries of Health.

There are two main limitations of this methodology. First, the self-reporting format may bias answers towards positive change. However, short of actually visiting the country to establish independent and objective evidence of change (which is expensive and probably not feasible), this is a reasonable method. Second, it is often difficult to firmly establish linkage between the evidence generated in a research study and policy and/or practice change.

References

1. Wiktor SZ, Sassan-Morokro M, Grant AD, et al. Efficacy of trimethoprim-sulfamethoxazole prophylaxis to decrease morbidity and mortality in HIV- 1-infected patients with tuberculosis in Abidjan, Cote d'Ivoire: a randomised controlled trial. Lancet 1999; 353: 1469-1475.

2. Zachariah R, Spielmann MPL, Chinji C, et al. Voluntary counselling, HIV testing and adjunctive cotrimoxazole reduces mortality in tuberculosis patients in Thyolo, Malawi. AIDS 2003; 17: 1053–1061.

3. Mwaungulu FBD, Floyd S, Crampin AC, et al. Cotrimoxazole prophylaxis reduces mortality in human immunodeficiency virus-positive tuberculosis patients in Karonga District, Malawi. Bull World Health Organ 2004; 82: 354–363.

4. Harries AD, Zachariah R, Chimzizi R, et al. Operational research in Malawi: Making a difference with cotrimoxazole preventive therapy in patients with tuberculosis and HIV. BMC Public Health 2011; 11: 1–9.

5. Harries AD, Kumar AMV, Satyanarayana S, et al. How can operational research help to eliminate tuberculosis in the Asia Pacific Region? Trop Med Infect Dis 2019; 4: 47.

6. World Health Organization. TB Research. Putting research into policy and practice: the experience of the Malawi National Tuberculosis Programme. WHO, Geneva, Switzerland. 1999. WHO/CDS/CPC/TB/99.268.

7. Ramsay A, Harries AD, Zachariah R, et al. The Structured Operational Research and Training Initiative for public health programmes. Public Health Action 2014; 4: 79-84.

8. Zachariah R, Guillerm N, Dar Berger S, et al. Research to policy and practice change: is capacity building in operational research delivering the goods? Trop Med Int Health 2014; 19:1068-1075.

9. Kumar AMV, Shewade HD, Tripathy JP, et al. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action 2016; 6: 44-49.

10. Tripathy JP, Kumar AMV, Guillerm N, et al. Does the Structured Operational Research and Training Initiative (SORT IT) continue to influence health policy and /or practice? Glob Health Action 2018; 11:1500762.

15   How to set up the operational research programme?

This chapter describes how to establish an OR programme or unit within a disease control programme and how to create capacity and human resources for OR activities. Examples of training initiatives are provided and suggestions on how to structure, monitor and evaluate OR projects are made.

15.1   How to set up the OR programme?

The overall purpose of OR is to provide an objective and scientific approach for solving public health problems and/or improving the performance of public health programmes. Adopting OR helps in minimising errors or biases in decision making due to guesswork, opinion or rule of thumb methods. OR can optimise the utilisation of available resources thereby improving the productivity and impact of public health interventions. (1)

Depending upon the requirements, OR can be used to bring improvements in the functioning of the health system (including hospitals and other health facilities) and the prevention and control of various diseases (malaria, tuberculosis, HIV, other tropical diseases, communicable and non-communicable diseases, etc.). It can also be used to address community issues, such as enhancing acceptability, increasing awareness, reducing stigma, etc. OR has the potential to address any issues related to public health and the health-care delivery system, the quality of services provided, managerial issues and issues at the community level.

There is an increasing thrust accorded by both international and national agencies to invest resources in OR and guide programme implementation in public health. (2) Therefore, setting up an OR programme within public health programmes or projects is important.

The following steps may be adopted to set up an OR programme.

- Obtain political and administrative commitment for integrating OR into public health programmes. This is important for the initial resource mobilisation and ensuring continuous flow of resources.

- Make OR into a distinct activity under the programmes or projects with a dedicated budget and human resources. This will ensure that prominence is given to OR and that OR is not overridden by other competing priorities.

- Periodically define OR priorities through a multi-stakeholder consultative process and communicate these priorities with all relevant stakeholders. The programme or project should be able to articulate and communicate the research priorities. This will give guidance to all prospective researchers on what they should focus on and will ensure judicious use of available resources to conduct the research most in need.

- Define and communicate clear mechanisms for calls for applications, OR protocol development, protocol review, administrative and ethics clearances and fund flow for initiating and completing OR.

- Understand the capacity to perform OR among various stakeholders and establish partnerships with national and international organisations and institutions to conduct OR or capacity building on OR.

- Periodically assess the performance of the OR activities and undertake corrective actions if the performance is sub-optimal (OR on OR…!)

- Have a well-defined mechanism to disseminate the results of all OR activities to all relevant stakeholders and provide technical support for policy formulation/practice change at the field level.

15.2 How to build capacity and appoint skilled research officers to the OR unit?

The health systems of many low- and middle-income countries share one common feature: they are overwhelmed with multiple diseases within a framework of limited human and financial resources. It is in these contexts that public health programmes need to embrace a culture or mindset of OR to understand what works and what does not work and find practical solutions to problems.

Several elements are needed to build and sustain OR capacity at national level, including having a mechanism to define and prioritise country-relevant research, building a critical mass of trained operational researchers who are embedded and retained within programmes and who can only conduct OR but also train others, making sure there is engagement and buy-in of decision makers and integrating these activities as part of country action plans and budgets. Effective dissemination including publishing in peer-reviewed journals is also needed. The latter serves as a quality control mechanism and is a recognised standard in medicine.

The driving principle for training at country level is that it must be practical and on- the-job training with hands-on mentorship and be accompanied with milestones and targets so that it is output oriented and the people who are undergoing training stay on course. One proven model that encompasses these aspects and has demonstrated significant success is the Structured Operational Research and Training Initiative (SORT IT). (3) This training which began as The Union/MSF OR training model in 2009 has now evolved into a global partnership coordinated by the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) and implemented with various partners.

SORT IT targets implementers, such as doctors, nurses, paramedical officers, data analysts and programme officers, especially in low- and middle-income countries often with little or no prior research experience.

Participants undergo training and conduct their research simultaneously while continuing to work in their respective projects or programmes. Each participant uses a relevant research project to learn the practical skills of how to write a study protocol, how to ensure quality-assured data capture and analysis, how to publish in a peer- reviewed journal and how to use the study findings to promote evidence-informed decision-making in public health. Participants must achieve milestones to move from one stage to the next and SORT IT courses are expected to achieve targets. Participants are supported with hands-on mentorship provided by experienced mentors.

Classic milestones for a SORT IT Course

- Milestone 1: Submission of protocol and the ethical review form within three weeks of completing module 1

- Milestone 2: Submission of the data documentation sheets within two weeks of completing module 2

- Milestone 3: Submission of proof of study completion and data collection about six weeks before module 3

- Milestone 4: Submission of a paper to a peer-review journal within four weeks of the end of module 3.

To maintain the quality and outputs of SORT IT courses, there are specific criteria to be fulfilled. These criteria are:

- The proposed course has modules that are based upon or adapted from SORT IT.

- Milestones and targets are systematically recorded as part of the implementation process.

- The 80% target for each of the above mentioned SORT IT milestones are monitored and reported upon. These targets have been introduced to ensure adherence to a rigorous "process" of quality control over a journey from defining a research question to its eventual influence on evidence-informed decision-making.

- On the administrative side, the course coordinator of a given course is required to update the focal person at TDR on course progress. The course details that need to be sent include participant details and their research titles, module evaluation scores, course status in relation to the SORT IT 80% targets and archives of study protocols, manuscripts and publications.

This model is primarily aimed at making countries data rich, information rich and action rich. The model (by the end of August 2023) has been expanded to 93 countries, trained close to 950 persons and resulted in hundreds of peer-reviewed papers. Importantly, nearly two-thirds of the research have contributed to a change in policy and or practice.

Another example is the Field Epidemiology Training Program (FETP) of the US Centers for Disease Control (CDC). Between 1980 and 2020, US CDC has helped train more than 18,000 disease detectives in over 80 countries through this flagship global programme. (4) Countries or public health programmes striving to embrace OR must be able to design a context specific mechanism for accommodating OR capacity building.

15.3 What are the management, monitoring and reporting structures?

The managers of OR programmes or units should take responsibility for the efficiency and effectiveness of OR. Management includes human resources, financial resources and knowledge and information management. Research teams often comprise members who have different disciplinary backgrounds, motivations and aspirations and different cultural backgrounds. Standard operating procedures for the management of the OR unit or component should be clearly articulated to ensure its smooth functioning. Some of the following best practices that can be adopted are as follows:

- Establish, agree, and communicate standards of performance and behaviour

- Establish style, culture, approach of the group - soft skill elements

- Monitor and maintain discipline, ethics, integrity and focus on objectives

- Anticipate and resolve group conflict, struggles or disagreements

- Enable, facilitate, and ensure effective internal and external group communications

- Identify and meet group training needs

- Give constructive feedback to the research groups on overall progress; consult with and seek feedback and input from the groups.

Some of the key aspects that OR programmes or units can monitor and report to donors and relevant stakeholders include:

- Number of OR projects/proposals received/initiated

- Number of OR projects completed

- Number of OR projects whose reports have been published in peer reviewed scientific journals

- Number of OR projects that have had an impact on policy and practice

- Number of OR related case studies showing the impact on policy and practice

- Number of trainings/workshops/people trained on research

- Number of institutions participating in research

- Proportion (%) of planned research expenditure disbursed/utilised

- Average/median time from commission to commencement of research studies

- Average/median time from commencement to completion of research studies

- Number of OR related presentations made in conferences.

References

1. Zachariah R, Harries AD, Ishikawa N, et al. Operational research in low-income countries: what, why, and how? Lancet Infect Dis. 2009; 9: 711–7. doi:10.1016/S1473-3099(09)70229-4.

2. UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, The Global Fund, World Health Organization, UNAIDS. Framework for operations and implementation research in health and disease control programs. 2008. Available: https://apps.who.int/iris/handle/10665/44686 (accessed 24 August 2023).

3. World Health Organisation. Structured operational research and training-initiative (SORT IT). Available: https://tdr.who.int/activities/sort-it-operational-research-and-training (accessed 24 August 2023).

4. US Centers for Disease Control and Prevention. Field epidemiology training program (FETP). Available: https://www.cdc.gov/globalhealth/healthprotection/fetp/index.htm (accessed 24 August 2023).

Appendix 1

Model consent form

Information sheets for potential participants should be brief and understandable by the people who are being asked to participate in the study.

The information must be provided in the home language of potential participants. An English translation is required for the ethics review panel.

The information must be presented in writing or verbally while avoiding medical and technical terms. If there is no alternative, such terms must be explained simply.

Researchers should pre-test the information sheet to see if it is really understood.

Recommended model

Title of study:

Principal investigator name:

Address:

Contact telephone number:

You are invited to take part in a research study. Please take some time to read the information presented here, which will explain details of this study. Please ask the researcher any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever, including health care now or in the future. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by ....(name the Ethics committees and health authorities who approved) and will be conducted according to ethical guidelines and principles of the International Declaration of Helsinki, as well as local ethical guidelines (...name these, if any are used)

---

[1]https://theunion.org/our-work/research/ethics-advisory-group/applications-for-eag-approval

What is this research study all about?

Explain briefly and simply using bullet points. Avoid medical or technical words. What procedures will be done and where, how long will these take and will return visits be needed?

Why have you been invited to participate?

Explain briefly how potential participants were selected (without detail about sampling processes).

What will your responsibilities be?

List, using bullet points, exactly what the participant will be asked to do, so they know what to expect and can decide about whether they are prepared to do it.

Will you benefit from taking part in this research?

Explain any possible benefits to individuals.

Will photographs be taken or tape recordings made?

Identifiers must be explained and specific consent asked for these procedures.

Are there in risks involved in your taking part in this research?

List any risks and how these will be managed.

Who will have access to the results of this study?

Explain briefly and simply how results will be kept confidential.

Where can participants get results of the study should they wish to have them?

Provide details of who can provide results.

Are there any costs involved and will you be paid to take part in this study?

Explain clearly, including any reimbursements.

Do you have any questions about the research?

If there is anything else that you want to know, if you have any further queries or encounter any problems you can contact.................................(give name of PI).

You will receive a copy of this information and consent form for your own records.

Appendix 2

Model consent form

All study participants must consent to participate voluntarily in a study.

They must preferably sign or give a verbal consent that they have received and understood information about the study including what it is about and what is expected of them.

The permission and collaboration of local civic/tribal leaders and health care providers is an important component of study preparation, although this never replaces individual participant consent.

Consent/Assent in the case of studies on children

When potential participants are children [as legally defined locally] the consent of the parents or guardians must be obtained in line with local custom and practice.

A child old enough to understand must agree to participate (assent). If such a child does not wish to participate, even if parents' consent, they should not be included.

Recommended model

Declaration by participant

By signing below, I... agree to take part in a

research study entitled .... (give name of study)

I declare that:

- • I have read this information and consent form and understand the contents.
- • I have had a chance to ask questions and all my questions have been adequately answered.
- • I understand that taking part in this study is voluntary and I have not been pressurized to take part.
- • I may choose to leave the study at any time and will not be penalized or prejudiced in any way.

Signed at (place) ....….........…………….. on (date) …………...………......................................

....Signature of participant or mark X if cannot sign ……………………

....Signature of witness

Declaration by researcher

I (name) .... declare that:

- I explained the information in this document to ……………………………....
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above.
- I did/did not use a interpreter (Sign the declaration below if an interpreter is used)

Signed at (place) ....….…......…………….. on (date) …………...………................

....
Signature of researcher   Signature of witness

Declaration by interpreter

I (name) .... declare that:

- I assisted the researcher (name) .... to
- explain the information in this document to (name of participant) … .... using the language medium of …............... (state which)
- I conveyed a factually correct version of what was related to me
- We encouraged him/her to ask questions and took adequate time to answer them
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her questions satisfactorily answered

Signed at (place) ....….…......……………. on (date) ………...…………………………

....
Signature of researcher   Signature of witness

The Union

International Union Against
Tuberculosis and Lung Disease

About The International Union Against Tuberculosis and Lung Disease
(The Union)

The Union is a scientific, technical and membership organisation. Established in 1920, The Union strives to end suffering due to tuberculosis and lung diseases, old and new, by advancing better prevention and care. We seek to achieve this by the generation, dissemination and implementation of knowledge into policy and practice. We aim to ensure that no one is left behind, people are treated equally and we have a focus on vulnerable and marginalised populations and communities.
A healthy world for all, free of tuberculosis and lung disease.