

Session- 16
Orientation Workshop for the Fresh Faculty Members

The Research Process: Asking the Right Question-I



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Research Should Be

- **Systematic** - All steps must be inter related- one to another
- **Logical** - Agreeing with the principles of logic
- **Empirical** -Conclusions should be based on evidences/observation

Features of a Research Design

- **A plan**
Specify the sources & types of information relevant to the research problem
- **A strategy**
Which approach will be used for gathering and analyzing the data
- **The time and budgets**
Most studies are done under these two constraints

Research Should Be

- Must do something which has not been done yet
- You need to be passionate
- If you do not have passion do not take research as profession
- You need to have patience

Characteristics of Research...

- **Objectivity**- It must answer the research questions
- **Replicable**- reproducible
- **Transmittable**
- **Quality control**- Accurate measurements
- All well designed and conducted research has potential application



Choose a subject area

- Choose an area of research
- Your interest
- Based on your experience
- Based on your reading
- Based on an idea
- Research Trend
- Originality

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Selecting Research Problem – (Where and How)

- Read, Read and read
 - Literature review
 - Library websites
 - Class discussions
 - Profession meeting (lab meetings)
 - Discussion with your professors and peers
- Selecting Topic:**
- Broad Area
 - Narrowing down

How to search....

- Literature search is a key step in performing good authentic research
- It helps in formulating a research question and planning the study
- But the available published data are enormous
- Choosing the appropriate articles relevant to the research question is an art
- It can be time-consuming, tiring and can lead to disinterest or even abandonment of search in between if not carried out in a step-wise manner
- Various databases are available for performing literature search

Literature search

Primary literature

- Primary sources are the authentic publication of research article, an expert's new evidence, conclusions and proposals (case reports, clinical trials, etc)
- Usually published in a **peer-reviewed** journal
- Peer means expert in the similar field
- Preliminary reports, congress papers and preprints also constitute primary literature
- Single blind and double blind peer review

Literature search

- What is a good article ?
- What is a good journal ?
- Predatory Journals ?
- Preferably do not search for research article using 'Google search'
- Lots of Craps

How to search...

Literature search is done to :

- Formulate research question and hypothesis
- Identify appropriate methodology
- Design of the study
- Protocols of experiments
- Population sampled and sampling methods
- Methods of measuring concepts and techniques of analysis
- **Relating your finding with the existing knowledge**

Different from search for research area selection or idea generation

Literature search

Secondary literature

- Secondary sources are systematic review articles or meta-analyses where material derived from primary source literature are inferred and evaluated

Tertiary literature

- Tertiary literature consists of collections that compile information from primary or secondary literature (reference books: dictionaries, encyclopedias, bibliographies, directories, atlases, and handbooks)

How to understand article quality

- Articles published in a good journal possibly is a good article
- What is a good journal ?
- There are several different metrics which are used to measure and evaluate the quality of scientific publications
- There are few good organizations does this job of evaluation or measurements

How to understand article quality

Scientific journals are measured and evaluated based on a series of criteria relating to the **quantity** of works published and the number of times that these works have been **cited**

Some important criteria :

- The number of works published
- The total number of citations received
- The average number of citations per work published
- The number of significant works published
- The number of citations received by the most frequently-cited works
- Indexing

Impact factor VS Cite score

- Elsevier launched a new journal metric, **CiteScore**, that takes direct aim at the domination of the **Impact Factor**, a product of **Clarivate Analytics** (formerly part of Thomson Reuters.)
- The two companies already have competing bibliographical citation databases in **Scopus** (Elsevier) and the **Web of Science** (Clarivate).
- **Cite score** is from **SCOPUS** and **Impact factor** is from data of **web of science** but cite score measuring on 3 years data while impact factor is from two years data.

Methods of literature search

Table 2: Web based methods of literature search

Resource	Web address
Search engines	
Google	http://www.google.com
Google Scholar	http://www.scholar.google.com
Yahoo	http://www.yahoo.com
Electronic source of database	
PubMed	https://www.nlm.nih.gov/pubmed
MeSH	http://www.ncbi.nlm.nih.gov/mesh
Medline (Medical Literature Analysis and Retrieval System Online)	https://www.nlm.nih.gov
CINAHL (The Cumulative Index to Nursing and Allied Health)	https://www.cinahl.com
Embase (Excerpta Medica Database)	https://store.elsevier.com/embase
SCOPUS	https://www.scopus.com/

Ranking of Journals

Journal Citation Reports (JCR): It includes publications reviewed by the most widely-cited experts in the world and covers approximately 200 different disciplines. JCR can be accessed online via the Web Of Science platform (WOS) and can be used to run online searches and look up the Impact Factor of a given journal or a group of journals and make comparisons between these. The impact factor is calculated annually by the Institute for Scientific Information (ISI). Clarivate Analytics (former name Thomson Reuter)

SCIMAGO Journal and Country Rank (SJR): This ranking emerged as a free-of-charge alternative to JCR. It analyses publications indexed in the SCOPUS database which is provided by the publisher Elsevier, dating from 1997 to the present. SJR enables users to run online searches using the Scopus platform, which is a paid-for tool, or using the **SCIMAGO Journal and Country Rank-SJR**. Each subject group of magazines is divided into four quartiles: Q1, Q2, Q3, Q4. Q1 is occupied by the top 25% of journals in the list.

Methods of literature search

Table 1: Methods of literature search

Protocol driven
Hand search of journal
Electronic search of databases
Snowballing
Reference chasing
Tracking citations
Personal knowledge
Existing theories and basics
Particular contacts and academic system
Offhand discovery: Such as finding a suitable paper when looking

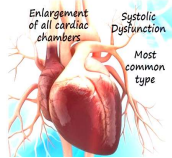
Literature search and finding gaps

An Example

- Research in biomedical field in Bangladesh is almost nil !!
- DGHS has some data on children vaccination and prevalence though not that authentic
- Because data collection system is not organized
- Sometimes data is biased
- Advanced research on onset, cause, diagnosis and treatment is absent
- Research method on treatment method is unethical
- No communication with Universities and research centers
- Superiority complex
- Research on cardiovascular disease (CVD) may be an good option in Bangladesh context

Dilated Cardiomyopathy (DCM)

- Dilated cardiomyopathy (DCM) is a disease of **heart muscle** and one of the important causes of **Heart Failure** manifests enlargement of heart with **left ventricular dysfunction**, **arrhythmia** and cause sudden **cardiac death**



Dilated cardiomyopathy is the most common type of cardiomyopathy

Global Burden and Bangladesh

- The global prevalence of DCM is **1 in 2500**, but recent study shows that the increasing ratio is **1:250** (Hershberger et al, 2013)
- Genetic makeup accounts **40%-50%** of cases for this multifactorial disease
- This disorder can occur at any **sex**, **race** and **geographical area**

There is no study on genetic cause or prevalence of DCM in Bangladesh

Literature search and formulating research question

Recently studies shows a steady increase in the rate of DCM patients in Bangladesh, even in the young (Hoque et al, 2019; Al Mamun, 2015)

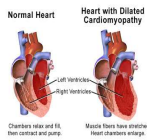
Al Mamun et al. (2015). Emerging burden of cardiovascular diseases in Bangladesh. *J atheroscl. thromb.* 30445.

Hoque et al. (2019). Clinical profile of patients with Idiopathic DCM in a Tertiary Care Hospital of Bangladesh. *Bangladesh Critical Care J.* 7(2), 86-89.

In different population the genetic mutations associated with DCM has been identified and are used for prognosis of the disease.

What Happens in DCM?

- The disease starts in the **left ventricle**, the heart's main pumping chamber
- The heart muscle begins to **dilate**, stretches and becomes **thinner** so the inside of the **chamber enlarges**
- As the heart chambers dilate, the heart muscle **doesn't contract normally** and cannot pump blood very well



As a result, **heart failure** can occur and lead to **heart valve problems**, **arrhythmias** (irregular heartbeats) and reduced ejection fraction

Causes of DCM

Table 2 Genes implicated in monogenic dilated cardiomyopathy and their cellular component

Gene	Protein	Function	Estimated contribution in DCM patients and phenotypic connectivity
Sarcomeric			
MYH7	Myosin 7 (beta-myosin heavy chain)	Muscle contraction	Non-mutating variants 5%
TNNI3P	Troponin T cardiac muscle (tropoin T2)	Muscle contraction	Non-mutating variants 5%
TTN ^{tr}	Titin	Extensible scaffold/molecular spring	Pathogenic variants 15-25%
DES ^{tr}	Desmosmin alpha 1 chain	Muscle contraction	0-2%
ANKRD1	Myosin-binding protein C, cardiac type	Muscle contraction	Mild hyperrophic cardiomyopathy gene; pathogenic association with DCM now less likely in light of population variation data [16]
TNNI3	Troponin C, slow skeletal and cardiac muscles	Muscle contraction	Mutations also associated with hypertrophic cardiomyopathy
TNNI3	Troponin I, cardiac muscle	Muscle contraction	Mutations also associated with hypertrophic cardiomyopathy
MYL2	Myosin regulatory light chain 2, ventricular cardiac muscle isoform	Regulation of myosin ATPase activity	Mutations also associated with hypertrophic cardiomyopathy
PIK3IP1	Phosphoinositide-dependent kinase-3	Sarcomeric organization	Mutations also associated with hypertrophic cardiomyopathy

More than 50 single genes are linked to

In different population the genetic mutations associated with DCM has been identified and are used for prognosis of the disease

Arshady HA, Momeni L. Dilated Cardiomyopathy: Genetic Determinants and Mechanisms. *Circ Res.* 2017;122(7):731-748. doi: 10.1161/CIRCRESAHA.116.300396 [Review]

Liu et al. Whole-Exome Sequencing Identifies Two Novel TTN Mutations in Chinese Families with Dilated Cardiomyopathy. *Cardiology.* 2017;128(1):10-14.

Pierro-Collini et al. Analysis of cardiac magnetic resonance imaging in 36,000 individuals yields genetic insights into dilated cardiomyopathy (USA). *Nat Commun.* 2020 May 7;11(1):2254.

Correia et al. Genomic study of dilated cardiomyopathy in a group of Mexican patients using whole-exome sequencing. *Mol Genet Genomics.* 2020 Nov 01;1-14.

Matsuura et al. Functional analysis of titin/connectin N2-B mutations found in cardiomyopathy (Japanese population). *J Muscle Res Cell Motil.* 2005;26(4-5):367-74.

Alkumrudi et al. Genetics and genotype-phenotype correlations in Finnish patients with dilated cardiomyopathy. *Eur Heart J.* 2012 Sep 13;33(36):2527-37.

Dai et al. Whole-Exome Sequencing Reveals Novel Genetic Variation for Dilated Cardiomyopathy in Palliative Chinese Patients. *Pediatr Cardiol.* 2019 Jun;40(5):950-957.

Rane et al. A novel arginine to tryptophan (R144W) mutation in troponin T (TTN) gene in an Indian mitochondrial family with dilated cardiomyopathy (TTCM). *PLoS One.* 2014 Jul 3;9(7):e101451.

Rick et al. Novel heterozygous truncating titin variants affecting the A-band are associated with cardiomyopathy and nonspecific muscular dystrophy (in USA). *Mol Genet Genomics.* 2020 Oct;393(10):1460.

Waldenström et al. Novel correlations between the genotype and the phenotype of hypertrophic and dilated cardiomyopathy: results from the German Competence Network Heart Failure. *Eur J Heart Fail.* 2011 Nov;13(11):1185-92.

Pinto-Pereira et al. Prospective implications of pathogenic truncating variants in the TTN gene (in Spain). *Int J Cardiol.* 2020 Jul;313:138-143.

Now choose an area of research

- Rationalize it.
- Rationalize your choice.
- Is it implementable?
- What are the probable barrier?
- How can you try to solve that?

End of Session

Formulating research question and setting up objectives

Research Question:

Can we predict DCM in early stages (prognosis) in Bangladeshi population?

General Objective:

Identification of TTN gene mutation in Bangladeshi population for prognosis of DCM

Specific Objectives:

1. Study the prevalence of DCM in Bangladesh
2. Identify the **genetic marker** in **TTN** gene among DCM patients in Bangladesh
3. Study for early **prognosis** by using these marker within DCM population in Bangladesh
4. Study the **pattern** of genetic variation in adult, postpartum and childhood DCM along with socio demographic **risk factors** responsible for DCM