# CILIOPATHY IN PEDIATRIC RESPIRATORY DISEASES: AN EVIDENCE BASED STUDY

***Thesis***

Submitted for partial fulfillment of master degree in
**Pediatric**

By

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# List of Abbreviations

| | |
|---|---|
| **EBM** | : Evidence based medicine |
| **NICU** | : Neonatal Intensive Care Unit |
| **PICO** | : The PICO Principle (population-Intervention-Control-Outcome) |
| **RCTs** | : Randomized Controlled Trials |
| **NLM** | : National Library of Medicine |
| **SR** | : Systematic review |
| **CAT** | : Critically Appraised Topic |
| **CATs** | : Critically Appraised Topics |
| **OR** | : Odd ratio |
| **CI** | : Conidendence interval |
| **RR** | : Relative risk |
| **NNT** | : Number needed to treat |
| **PCD** | : Primary ciliary dyskinesia |
| **MME** | : Mucociliary Escalator |
| **MMC** | : Mucociliary clearance |
| **NO** | : Nitric oxide |
| **RSV** | : Respiratory syncital virus |
| **FVC** | : Forced vital capacity |
| **SVN** | : Small volume nebulizer |
| **CFTR** | : Cystic fibrosis transmembrane conductance Regulator |
| **CF** | : Cystic fibrosis |
| **NCG** | : National commissioning group |
| **rhDNase** | : Recombinant human DNase |
| **JBTS** | : Joubert syndromes |
| **MKS** | : Meckel-Gruber syndrome |
| **SLS** | : Senior-loken syndrome |
| **OFD** | : Orofacial digital syndrome |
| **LCA** | : Leber's congenital amaurosis |
| **BBS** | : Bardet-Biedi syndrome |
| **ALS** | : Alstrom's syndrome |

# List of Abbreviations (Cont.)

**JATD** : Jeune asphyxiating thoracic dystrophy
**EVC** : Ellis Van Creveld syndrome
**PKD** : Polycystic kidney disease
**STARD** : Standard for reporting of diagnostic accuracy
**CONSORT** : Consolidated Standards of Reporting

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# Introduction

Respiratory disease is a medical term that encompasses pathological conditions affecting the bronchi, bronchioles, alveoli, pleura and the nerves and muscles of breathing. Respiratory disease range from mild and self limiting, such as the common cold, to life threating entities like bacterial pneumonia, pulmonary embolism and lung cancer ***(Bush, 2010)***.

Microscopic cilia are present on the mucosal surface of the upper and lower respiratory tract, which beat in a coordinated fashion at 12-18 Hz, thereby creating a flow of mucus which continuously removes inhaled bacteria and airway debris and maintaining the sterility of the lower respiratory tract ***(Barlocco et al., 2009)***.

When the cilia beat abnormally, such as in immotility or dyskinesia either due to abnormally or the ultra structure or for unknown reason, patient could suffer from sinusitis, bronchiectasis, deafness, infertility and sometimes situs inversus ***(Afzellius, 2009)***.

Defective ciliary ultra structure and impaired mucociliary clearance play an important role in the development of respiratory disease and sinusitis ***(Buchdahl, 2010)***.

A ciliopathy is a genetic disordered of the cellular cilia or the cilia anchoring structures, the basal bodies, or of ciliary function. Although ciliopathies are usually considered to involve proteins that localize to the primary cilia or centrosomes, it is possible for ciliopathies to be associated with proteins such as XPNPEP3, which localizes to mitochondria but is believed to affect ciliary function through proteolytic cleavage of ciliary proteins ***(Johnson et al., 2009)***.

Cilial dyskinesia shares its root causes with a number of other genetic conditions that affect the cilia known as ciliopathies. The symptoms of the condition are highly treatable if ciliary dyskinesia is diagnosed in childhood. Unfortunately, the symptoms are similar to many normal childhood illnesses. So the diagnosis is often missed until later in life. When more drastic treatment (including massive doses of antibiotic and extreme cases, a lung transplant) are necessary ***(Gardiner, 20010)***.

A systematic review is a literature review focused on a research question that tries to identify, appraise, seled and synthesis all high quality research evidence relevant to the question. Systematic reviews of high quality randomized controlled trial are crucial to evidence based medicine. An understanding of systematic reviews and how to implement them in practice is becoming mandatory for all professional involved in delivery of health care ***(Herman et al., 2009)***.

Evidence based medicine (EBM), has been launched as a process by means of which advances in medical research may come into practical use so as to yield safe, better and more cost effective health care ***(Nordenstrom, 2010)***.

# Aim of the Work

The aim of this study is to carry out a review about ciliopathy in pediatric respiratory disease.

# Chapter ( 1 )
# Evidence Based Medicine (EBM)

## Introduction:

Physicians are judges. They take decisions and doing recommendations which concern people's life. As it was said by one of the greatest physicians in history; "It is a capital mistake to theorize without having the best evidence', so it will be a great mistake to do medical decisions without powerful scientific evidence.***(Shaheen, 2009).***

Evidence Based Medicine (EBM) is still a BIG puzzle to physicians either in understanding it or in its practice. However, there is an increasing need for it in medical profession. Today students and practitioners of medicine have a huge amount of information resources at their finger tips, yet many feel uncertain about how to find the right articles to read. Information technology (IT) and the internet have resulted in such extraordinary availability of information. The application of EBM practice could be defined as the judicious selection process through this informative invasion.***(Greenhalgh, 2010).***

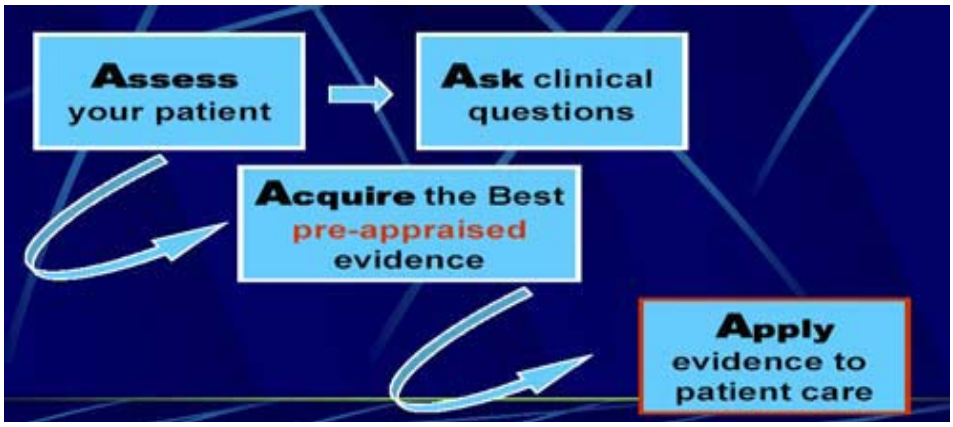


**Fig.(1) : General strategy of EBM *(Shaheen, 2009 ).***

## Definition:

Evidence based medicine (EBM), is commonly defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient" ***(Justice, 2009).***

Evidence based medicine (EBM), has been launched as a process by means of which advances in medical research may come into practical use so as to yield safer, better and more cost-effective health care.

Clinical expertise refers to the clinician's cumulated experience, education and clinical skills. Patient values mean the unique preferences, concerns and expectations. The best evidence is usually found in clinically relevant research that has been conducted using sound methodology (figure 1) ***(Sestini and Irving,2009).***

## This description has several key components:

- Clinical care: EBM allows clinicians to combine the best of patient assessment with clinical research evidence to assist in patient care.
- Clinical practice guidelines: EBM can help define the strength of evidence supporting a particular practice, and help to rank the importance of interventions.
- Quality improvement**:** variations in practice can be assessed according to EBM guidelines to assist in minimizing inappropriate practice variation and maximizing the application of useful treatments.

- Clinical research: an assessment of the evidence will highlight those areas of clinical practice where evidence is lacking. This information can be used to plan future research studies to provide evidence for or against treatment. ***(Nordenstrom, 2009).***

## How to practice Evidence-based Medicine?

The EBM process consists of four steps: "FIRE"

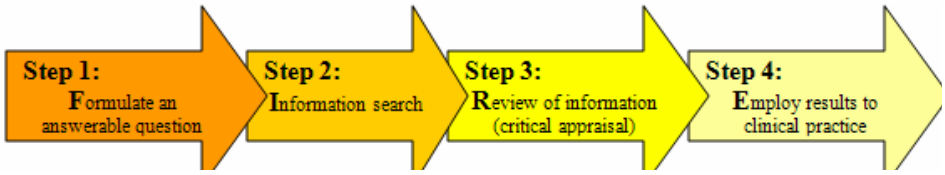


**Fig. (2) : Steps of EBM.** ***(Shaheen, 2009).***

Remember FIRE

## Step 1 :

### *Formulate an answerable question :*

It starts with asking a question in a way that can be answered. This involves defining the relevant population, the intervention and control groups comparison, the relevant outcomes, and the optimal design to answer the question (A general formula for the PICO question).

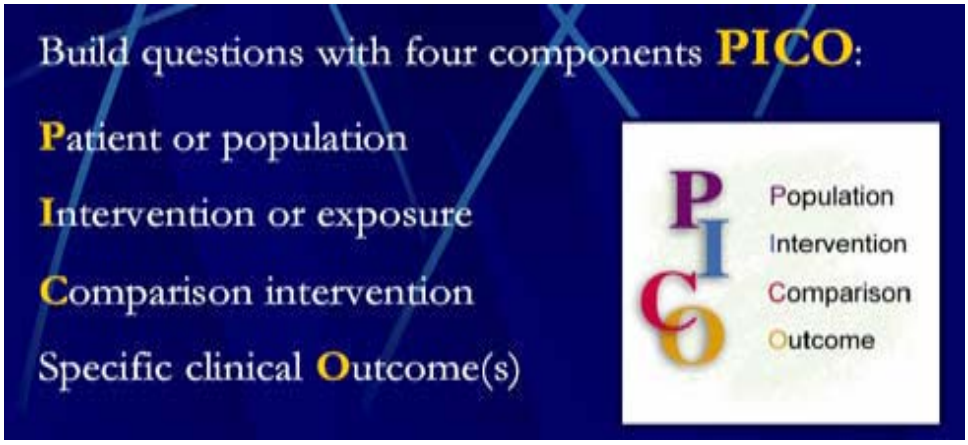


**Fig. (3) : General formula for question.** ***(Shaheen, 2009).***
Remember PICO.

**Ask yourself important clinical questions about your patients:**

- Therapy Question: Concerning the effectiveness of a treatment
- Prognosis Question: Concerning outcome of a patient with a particular condition.
- Diagnosis Question: Concerning the ability of a test to predict the likelihood of a disease.
- Harm Question: Concerning the likelihood of a therapeutic intervention or exposure to cause harm.

Once you created a question, this will affect where you look for the answer and what type of research you can expect to provide answer**.** ***(Shaheen, 2009).***

## Step 2 :

## Information search :

It involves finding the best available evidence, efficiently by means of electronic database searches. The key to efficient searching is to know where reliable and relevant information can be found most often. .***(Crombie, 2009).***

**What is the "Evidence" in Evidence-Based Medicine ?**

We must learn to find and evaluate the best evidence on which to base our practice. Frequently, the best evidence available is not the best evidence possible ***(Geddes,2009)***.

The quality strength of the evidence ranges from systematic reviews of multiple well-designed randomized controlled trials RCTs to the opinion of respected authorities (based on clinical evidence, descriptive studies, or reports of expert committees). RCTs are limited in their ability to evaluate the long-term consequences of therapy and are of no use in evaluating issues such as exposure to chemical or industrial hazards ***(Legg, 2008).***

We need to develop the habit of looking for the current best answer as efficiently as possible to manage pressing problems. Search strategies have been developed to use them efficiently which are a science in themselves ***(Mullen et al., 2008).***

High levels of evidence will not exist for all clinical questions because of the nature of medical problems and research and ethical limitations. Adding methodology terms and clinical filters to subject terms will result in the most efficient and optimal retrieval in terms of finding the highest level of evidence in answering clinical questions ***(Jo. Dorsh, 2010).*** The premier resource for searching is the secondary