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Imam Reza General Hospital Newsletter

Tabriz University of Medical Sciences

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Tabriz University of Medical Sciences, Tabriz, Iran

Imam Reza General Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

In this issue we read:

An Overview of the Events of the Center, the Articles of the Respected Professors and the International Educational Programs

• **Mojtaba Mohammadzadeh**
Assistant Professor of Anesthesiology and Intensive Care Medicine
The head of Imam Reza General Hospital, Tabriz, Iran and the Scientific Editor of the congress

The honorable achievement of the clinical research development unit of Imam Reza General Hospital in Tabriz, Iran

Fortunately, the clinical research development unit at Imam Reza General Hospital in Tabriz has achieved the fourth national rank among top universities for the second time. This significant achievement is an important sign of the scientific capabilities and high research potential of the center's professors, residents, and students. I would like to express my gratitude to the esteemed Deputy Dean of Education and Research of the center, the respected head of the clinical research development unit of Imam Reza General Hospital, and the expert staff of the deputy of education and research of the center. I kindly request the respected professors and students to further support the clinical research development unit at Imam Reza General Hospital in Tabriz. This can be done by acknowledging the affiliation of this unit in the acknowledgment section of articles and dissertations that utilize data from Imam Reza General Hospital in Tabriz. This will advance this unit and help achieve top rankings for Imam Reza General Hospital in Tabriz. Additionally, the Persian and English text of affiliation of this unit to be included in articles is as follows:

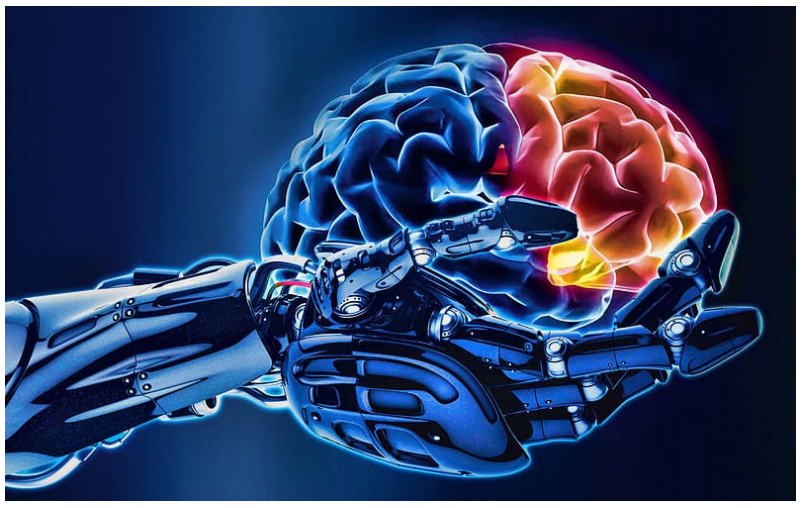
Acknowledgment
We would like to appreciate of the cooperation of Clinical Research Development Unit, Imam Reza General Hospital, Tabriz, Iran, in conducting of this research.

Establishment of the Artificial Intelligence Laboratory at Imam Reza General Hospital in Tabriz

• **Hassan Soleimanpour**
Editorial Message
Editor in Cheif
Professor of Anesthesiology and Critical Care, Subspecialty in Intensive Care Medicine (ICM), Clinical Fellowship in EBM, Fellowship in Trauma Critical Care and CPR
Deputy Dean for Education and Research, Imam Reza General Hospital, Tabriz, Iran

We thank God that with the comprehensive support of the esteemed Vice chancellor for research of the university and the special attention of the respected Dean of Imam Reza General Hospital in Tabriz, the Artificial Intelligence Laboratory at Imam Reza General Hospital in Tabriz has been established and is on the verge of becoming operational. Some applications of artificial intelligence are to enhance healthcare quality, assist in diagnosing and treating diseases, and bring transformation in this field. Traditional medicine has undergone substantial changes with advanced artificial intelligence technology. Furthermore, artificial intelligence technology has significantly contributed to developing pharmaceuticals, Health Information Technology , and education in the field of medicine. Artificial intelligence enables computers to think, reason, and solve problems like humans. Below are the most important capabilities of artificial intelligence in medicine:

Optimization of the screen and diagnosis to treatment of the disease and follow-up care, patient care, Reduction of errors, Reduction of healthcare costs, Increased interaction between doctors and patients, More accurate decision-making in therapeutic and clinical functions, Creation of hospitals with the help of robots, Imaging and medical diagnosis, Management of hospital resources and data, Robotic-assisted surgery, Monitoring of chronic diseases, and Visual quality inspections of medical equipment



It is important to acknowledge that despite artificial intelligence's many benefits in health, there may also be potential issues and drawbacks linked to its use. One of the most significant drawbacks is the high cost of implementing and installing the necessary infrastructure and equipment. This issue may deter healthcare center officials from adopting this technology. Other significant disadvantages that artificial intelligence may present in medicine include the complexity of implementing the infrastructure. In many cases, to ensure that this infrastructure is established correctly, several expert and experienced specialists are required. Issues such as maintaining privacy and data security, the potential for bias in artificial intelligence algorithms, data collection, and the risk of unemployment caused by technology are among the challenges and concerns regarding using artificial intelligence in the medical sciences. In conclusion, it is hoped that using artificial intelligence in medicine will significantly contribute to reducing the costs of hospitals and healthcare centers.

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A Century of Insulin Innovation

• **Afshin Gharekhani**
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It has been nearly 100 years since insulin was first isolated and purified as a lifesaving hormone for people with diabetes. During this remarkable journey, insulin products have undergone significant transformations. Initially extracted from animals, production has now shifted to cutting-edge DNA technology. This advancement has led to a dramatic reduction in inflammatory reactions and side effects previously associated with animal-derived insulins.

Pharmaceutical advancements, spearheaded by dedicated researchers, have yielded insulins with more precise and predictable durations of action (half-lives). This empowers physicians to more effectively regulate blood sugar levels. The landscape of insulin products has expanded beyond a limited range of options. In addition to various generic formulations, pharmaceutical companies offer numerous brand-name derivatives. While understanding the intricacies of each product is valuable, for simplicity, we can categorize insulins into two main classes: fast-acting and long-acting. Within these categories, further subcategories exist, such as very fast-acting, medium-acting, and very long-acting. However, for the purpose of this article, we will focus on these two primary classifications.

Rapid-Acting Insulins

Modifications to the amino acid sequence of the insulin protein have resulted in rapid onset of action and a short duration of effect in these insulins. As a reminder, insulin is a protein comprised of 81 amino acids, structured with two alpha (α) and beta (β) chains. Most of these modifications target the terminal end of the beta chain. Regular human insulin tends to form hexamers (clusters of six molecules) upon subcutaneous injection, which then slowly break down into monomers (single molecules). This process delays the onset of insulin action. To address this, changes have been made to the sequence of terminal amino acids. Additionally, special excipients (inactive pharmaceutical ingredients) are employed to prevent hexamer formation during injection. These strategies enhance the release rate of monomers, thereby accelerating the onset of action for rapid-acting insulins.

Aspart, glulisine, and lispro insulins fall into this category and exhibit similar pharmacokinetic profiles (absorption, metabolism, and elimination of the drug). These rapid-acting insulins typically begin to work within 10 to 20 minutes after injection, making them suitable for administration around mealtimes and allowing for dose adjustments based on individual needs. However, their lifespan is limited to 4 to 6 hours, after which they are eliminated from the bloodstream. An important consideration is the peak plasma concentration, which occurs roughly one hour after injection. This peak can potentially contribute to side effects like hypoglycemia, particularly in cases of incorrect dosing. It›s crucial to note that insulin promotes the shift of potassium from the extracellular space into the cells. This can be a life-threatening complication for patients with heart failure or those at risk of arrhythmias.

Long-Acting Insulins

NPH (Neutral Protamine Hagedorn) insulin was the first long-acting insulin commercially available. While offering a longer duration of action compared to regular insulin, it falls under the category of moderate-acting insulins. Notably, NPH insulin does not involve modifications to the protein or amino acid sequence of insulin itself. Instead, it achieves its extended effect through the addition of protamine, a marine protein derived from cold-water fish like sardines and salmon, and zinc. This combination creates a crystalline, white suspension. Upon injection, this insulin forms a protein depot within the body from which insulin is gradually released. The breakdown of protamine by enzymes (proteases) controls the release of insulin. When formulated correctly, NPH insulin typically does not generate a distinct peak in blood plasma concentration. While the onset of action takes 3 to 4 hours, the duration of effect is highly variable (ranging from 6 to 23 hours) and heavily influenced by the injected dose.

Insulin Glargine: Unlike NPH insulin, which maintains its natural amino acid sequence, insulin glargine is engineered with modifications to both alpha (α) and beta (β) chains. These modifications promote the formation of hexameric polymers, delaying the conversion of insulin protein into active monomers. This translates to a slower onset of action (around 4-3 hours to become a monomer) compared to NPH insulin. However, the duration of effect is significantly extended, ranging from 18 to 30 hours (typically 24 hours) depending on the injected volume. It›s important to note that insulin glargine is available in a higher concentration (300 units per milliliter) compared to the standard 100 units per milliliter for NPH insulin. This increased concentration can slightly influence both the onset and duration of action, resulting in a slower start and a longer-lasting effect.

Fatty Acid-Formulated Insulins

In the constant pursuit of precise blood sugar control, researchers have developed insulins formulated with fatty acid agents. These insulins aim to provide a more consistent and predictable duration of action compared to traditional options. This consistency is achieved by combining insulin protein with a fatty acid, facilitating a controlled and sustained release of insulin into the bloodstream. Ideally, this approach offers a constant level of insulin with a reliable lifespan, less dependent on injection volume and other variables.

Two primary insulins fall within this category:

Detemir Insulin: This was the first product to utilize this fatty acid formulation technique. It employs a -14carbon fatty acid called myristic acid. The onset of action for Detemir insulin is typically between 3 and 4 hours. However, it›s important to note that due to its pioneering nature, Detemir exhibits a variable duration of effect. Lower doses can result in a range of 6 to 23 hours, while higher doses tend to offer a more stable duration of around 22 hours.

Degludec Insulin: Degludec insulin represents a significant advancement over Detemir. It incorporates a -16carbon fatty acid instead of the -14carbon myristic acid and also features modifications to the beta (β) cluster of the insulin protein. These advancements culminate in the most predictable and consistent duration of action among all basal insulins. This advantage makes degludec insulin a particularly valuable option for achieving precise blood sugar control in situations like pregnancy or managing diabetes in individuals with kidney disease. Today, insulin products are available with different types and different domestic and foreign brands in the pharmaceutical market of Iran. This accessibility empowers physicians with more options for accurate blood sugar control. This brief introduction to insulin products can serve as a springboard for further in-depth exploration.

The Essence of Hospital Pharmaceutical Care Units in Pharmaceutical Care

• **Sama Samankan**
Clinical pharmacy resident
Tabriz University of medical sciences, Tabriz, Iran

The face of modern-day health care is radically transforming, with increasing focus on patient-centered care and medication safety. In such an environment, clinical pharmacists play an important role as part of the health care team, especially in hospital Pharmaceutical Care Units (PCUs). The hospital sector is where PCUs exist to optimize the use of medication and ensure the best outcomes for the patients.

• **Optimizing Medication Safety:** A Core Function One of the primary functions of clinical pharmacists in PCUs is medication safety. This is a comprehensive activity from medication review to the discharge of the patient.

• **Medication Reconciliation:** When patients are admitted to the inpatient unit, clinical pharmacists conduct an extensive medication history. This process is where all the patient›s current medications are verified- both prescription and over-the-counter medications and supplements and herbal products. The main rationale behind this activity is to align the patient›s medications from the community setting with the inpatient admission medication orders to identify potential medication errors and adverse drug events.

• **Therapeutic Dosing:** Pharmacists interpret patient-specific parameters to ensure medications are dosed to reach the therapeutic range. These parameters include age, weight, renal function, and potential drug interactions. In the elderly, for instance, modifications in renal function and/or metabolism will be factors that affect drug disposition and drug elimination. Such parameters are typically modified in the elderly adult due to geriatric processes. At this juncture, pharmacists establish the necessary medication dose adjustments to deliver an optimally safe and effective therapeutic strategy for managing the older adult. The same will be for a patient›s weight. As the weight differs, so does the drug distribution and metabolism. Pharmacists will consider the patient›s weight to provide the required dosages to avoid probable under-treatment or over-treatment. Renal function is an additional vital factor. As kidneys facilitate elimination of various drugs, pharmacists check kidney function to make the necessary medication adjustments to provide the appropriate doses, thus eliminating further accumulation of medications in the patient›s body. Besides patient-specific factors, pharmacists identify any probable drug interactions that may lead to safe and effective dosing. Some medications interact with others to result in the inhibition or metabolism and accelerated metabolism of others. It is from the mechanisms of actions of various drugs, the possibility of enzymes inhibition or induction, and common metabolic pathways that pharmacists are able to determine which interactions may be problematic. Pharmacists, by taking such factors into consideration, can make drug dosing regimens individual to each patient to enable the maximum level of therapeutic effect to be achieved and the least possibility of adverse reactions occurring.

• **Medication Selection and Monitoring:** Clinical pharmacists collaborate with clinicians to select the most appropriate medications for a patient›s specific condition, balancing several things. Among these is the relative efficacy of different medications for the target disease, the potential side effects and their severity, costs of medications, and individual preferences and adherence issues for the patient. Pharmacists, being a part of Pharmacoeconomics, evaluate the cost-effectiveness of different possible medication options to be used by the patient in question, thereby ensuring value for money. They also consider the medical history of the patient, allergies, and potential for drug interactions in medication selection. In addition, adherence to medication regimens is a critical component of successful treatment. Pharmacists assess a patient›s ability to follow a medication regimen, taking into consideration the complexity of the regimen, the burden of pills, and side effects. They are able to recommend less frequent dosing of medications, with less severe side effects, or otherwise educate the patient toward better adherence.

• **Therapeutic Drug Monitoring:** Other treatments would need close monitoring of blood levels to assure effectiveness and that a therapeutic dose, with minimum risk of toxicity, is being provided. In these situations, the clinical pharmacists use their knowledge to analyze the test findings and provide advice on adjusting prescription dosages.

• **Enhancing Patient Care:** Beyond Medication Management
The expertise of clinical pharmacists extends beyond ensuring medication safety. They play a pivotal role in enhancing the quality of patient care through a variety of initiatives.

• **Direct Patient Care:** Clinical pharmacists work collaboratively with physicians and nurses to develop personalized medication plans for each patient. They actively participate in rounds, providing valuable insights into medication selection, dosing, and potential side effects. Additionally, they educate patients on their medications, empowering them to become active participants in their own healthcare.

• **Disease Management:** Clinical pharmacists possess in-depth knowledge of specific disease states. They contribute significantly to disease management programs by providing medication expertise and tailoring treatment plans to optimize patient outcomes in areas such as diabetes, heart failure, and chronic obstructive pulmonary disease (COPD).

(continued on next page)

(Sama Samankan Cont.) • **Patient Education and Counseling:** Effective communication and patient education are central to a clinical pharmacist›s role. They provide patients with clear and concise information about their medications, including potential side effects, proper administration techniques, and the importance of medication adherence. This empowers patients to make informed decisions about their healthcare and manage their conditions effectively.

• **Discharge Planning and Medication Management:** In preparation for discharge from the hospital, pharmacists work with the discharge planning team to ensure patients understand their medications, have a clear medication plan, and can access necessary refills upon returning home. This comprehensive approach ensures a smooth transition from hospital care to home care.

Driving Healthcare Efficiency: A Catalyst for Cost-Effectiveness
The contributions of clinical pharmacists in PCUs extend beyond patient care, positively impacting healthcare efficiency and cost-effectiveness.

• **Medication Cost Management:** Clinical pharmacists work closely with physicians to identify cost-effective treatment options while ensuring therapeutic efficacy. They can recommend generic medications when appropriate and advocate for the most cost-effective medication based on individual patient needs.

• **Reduced Readmissions:** Medication-related issues are a significant contributor to hospital readmissions. The proactive interventions of clinical pharmacists in PCUs, such as medication reconciliation and patient education, can help to reduce readmission rates by minimizing medication errors and ensuring smooth transitions of care.

• **Improved Resource Utilization:** Clinical pharmacists contribute to the efficient use of hospital resources by identifying and preventing medication-related complications that could lead to extended hospital stays or the need for additional diagnostic procedures.

Conclusion: Indispensable Partners in Patient Care
Clinical pharmacists in PCUs play an indispensable role in ensuring medication safety, optimizing patient care, and driving healthcare efficiency. Their expertise in medication management, coupled with their focus on patient education and collaborative care, contributes significantly to improved patient outcomes and a more cost-effective healthcare system. As the healthcare landscape continues to evolve, the essential role of clinical pharmacists in PCUs will undoubtedly become even more prominent.

Metabolic Issues in Polycystic Ovary Syndrome

• **Mahsa Malekian**
Assistant Professor of Endocrine research center
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The polycystic ovary syndrome (PCOS) is an important cause of both menstrual irregularity and androgen excess in women.
PCOS is one of the most common endocrinopathies in women of reproductive age, affecting between 6.5 and 8 percent of the women.

Metabolic Issues
1. Obesity and insulin resistance; 2. Nonalcoholic fatty liver disease; 3. Metabolic syndrome; 4. IGT/type 2 diabetes; 5. Sleep apnea; 6. Dyslipidemia.

Obesity and insulin resistance
Most investigators have found that at least one-half of the women with PCOS are obese. Most women with PCOS, compared with normal women, are also hyperinsulinemic and insulin resistant, independent of obesity. Hyperinsulinemia contributes to the hyperandrogenism both directly through stimulation of androgen biosynthesis in the ovarian theca cell and indirectly through its suppressive effects on sex hormone-binding globulin (SHBG) production by the liver.
Reduction in the degree of insulin resistance and hyperinsulinemia with weight loss, metformin, or a thiazolidinedione is associated with the decreased androgen levels in women with PCOS.

Nonalcoholic fatty liver disease
The prevalence of nonalcoholic fatty liver disease (NAFLD), including nonalcoholic steatohepatitis (NASH), may be increased in women with PCOS.
According to the results from a previous study, 21 out of 70 women with PCOS (30 percent) had elevated serum alanine aminotransferase (ALT) Concentrations. In a population-based study investigating over 18,000 adults, in contrast, an abnormal ALT was seen in only 2 percent of all women, 5 percent of the women with type 2 diabetes, and 7 percent of the obese women.

Metabolic syndrome
According to the most recent National Health and Nutrition Examination Survey (NHANES) report, the prevalence of the metabolic syndrome in normal women aged 39-20 years was approximately 18 to 19 percent.
Using the same diagnostic criteria, its prevalence among women with PCOS has been found to be much higher.
The results from a retrospective study showed that 43 percent of the PCOS patients had metabolic syndrome, roughly twofold higher than that of the age-matched women in the general population.
According to another study, the prevalence of metabolic syndrome was approximately 47 percent in women with PCOS, whereas it was 4 percent in age matched (but not weight-matched) controls with regular menses and no Hirsutism.

IGT/type 2 diabetes
The risk of type 2 diabetes is increased in PCOS, particularly in women with a first-degree relative with type 2 diabetes. In a study on 122 obese women with PCOS, 45 percent of them had either impaired glucose tolerance (35 percent) or type 2 diabetes mellitus (10 percent) by age 40.
In a subset of 25 women undergoing a repeat oral glucose tolerance testing (OGTT) after a mean of 34 months, 40 percent experienced a deterioration.
In another study on 71 women with PCOS, the annual conversion rate from normal glucose tolerance to IGT was found to be 17 Percent.
Women with PCOS and a family history of type 2 diabetes may have an impairment in insulin secretion and insulin resistance.
This suggests that there is a heritable component to beta cell dysfunction among families of women with PCOS.
Insulin resistance is recognized as a major risk factor for type 2 diabetes. Factors such as obesity and family history of type 2 diabetes can increase the risk of diabetes in PCOS.
Women with PCOS show higher risk of gestational complications, such as miscarriage, gestational diabetes mellitus (GDM), hypertension, and preeclampsia.

Sleep apnea
Healthcare professionals should be aware that women with PCOS have significantly higher prevalence of obstructive sleep apnea compared with women without PCOS, independent of BMI. Women with PCOS should be assessed for symptoms of obstructive sleep apnea. In one study, %44 of women with polycystic ovary syndrome experienced obstructive sleep apnea, which exacerbates insulin resistance and can lead to type 2 diabetes. In another study, %56 of women with this syndrome had sleep apnea compared to %19 in the control group, and there was also a higher prevalence of obesity and insulin resistance in this group.

Dyslipidemia
Most studies on women with PCOS have demonstrated low high-density lipoprotein (HDL) cholesterol and high triglyceride concentrations, consistent with their insulin resistance, as well as an increase in low-density lipoprotein (LDL) cholesterol.
According to a review investigating 195 obese and non-obese women with PCOS as well as 65 weight matched controls, the serum LDL cholesterol was increased in both obese and non-obese PCOS groups compared with controls. According to another study on 398 women with PCOS, the prevalence of abnormal lipid parameters was extremely high:
Total cholesterol ≥200 mg/dL : 35 percent
LDL ≥130 mg/dL : 31 percent
HDL <35 mg/dL : 15 percent
Triglycerides >200 mg/dL: 16 percent
Women with PCOS are also more likely to have an increase in small, dense LDL particles when compared with women of similar BMI and insulin resistance without PCOS. Small, dense LDL is strongly associated with an increased risk of coronary heart disease (CHD).

Therapeutic Hypothermia in severe traumatic brain injury

• **Hassan Soleimanpour**
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A type of loss of consciousness in which the person does not respond to external and painful stimulation or shows a weak reaction. Hypothermia is a method in which we preserve the brain cells of the patient and neurological cells help to regenerate neurons. The patient can fully recover through this method, which is only performed at ICU7, Imam Reza General Hospital, Tabriz, Iran.

Is treatment and recovery from coma possible?

Prof. Hassan Soleimanpour: Hypothermia is an effective and comprehensive protocol for patients with severe traumatic brain injury who are in coma. I hope we can publish the results of this study in the near future in reputable medical journals. Using a new method, the medical team at Imam Reza General Hospital in Tabriz has succeeded in bringing severely traumatized patients back to life.

• **Sarvin Sanaie**
Assistant Professor of Nutritional Sciences
Tabriz University of Medical Sciences, Tabriz, Iran

Could you please introduce yourself?

I am Sarvin Sanaie, MD, PhD in Nutrition. I am an assistant professor at the Aging Research Institute of Tabriz University of Medical Sciences. Besides the clinical and educational tasks that I do, I perform some research in my fields of interest consisting of all the study types but today I (continued on next page)

(Sarvin Sanaie Cont.) wanna focus on systematic reviews and meta-analysis which indeed is the title of my educational program:

What is a systematic review and why it is performed?
A Systematic Review is defined as a review of evidence on a clearly formulated question that uses explicit methods to Identify, Select, Appraise, and Synthesize results from similar but separate studies. Not all systematic reviews would have a meta-analyses. A meta-analysis is the statistical method of analyzing a large collection of results from individual studies.

There are many online and offline courses for systematic reviews; what makes your course different and outstanding?
You are totally right. What makes us different can be highlighted briefly as the method of our training. If I want to explain what I mean I should say that as you said there are various classes, workshops, and online courses about this issue but they just teach you the basics of performing a systematic review theoretically and finished. Here, in addition to these theoretical courses, we will practically conduct a systematic review from A to Z with anyone who has attended the classes. I mean my team and I will be in contact with the participants at any stage of the research from its beginning which is the selection of a research title up to the end which is submitting the article in a journal.

You just said you have a team; can you talk about your team?
Of course, my team consists of 4 recently graduated medical students and me. Sama Rahnemayan, Paria Tahmasbi, Salar Hosseini, and Amirreza Naseri are these young physicians who work with me in performing the systematic reviews and in training for this course. These 4 young physicians have totally published more than 100 systematic review articles in the last 3 years.

What are the objectives and goals of your course?
Upon successfully completing this course, participants will be able to:

1- describe the steps in conducting a systematic review
2- formulate an answerable question using the PICO framework which means participants, interventions, comparisons, and outcome
3- defined the inclusion and exclusion criteria
4- perform a systematic search for evidence
5- extract data from reports
6- critically assess the risk of bias
7- finally perform and interpret the results of meta-analyses

Which modules will be covered in this course?
There are 6 modules in this course
1- Introduction
To get the ball rolling, we›ll take a broad overview of what to expect in this course and then introduce the high-level concepts of systematic review and meta-analysis and take a look at who produces and uses systematic reviews.
2- Framing the Question
3- Searching Principles
Finding the evidence, key sources, search strategy
4- Assessing the risk of bias
5- Qualitative and quantitative Synthesis
6- Wrap Up and Final Peer Review Assignment
In this final module, we›ll wrap up with a look back at the key concepts covered over the past few weeks. Afterwards, we will submit the final Peer Review Assignment.

How long is your course?
This course will be held in two steps. The first one is the theoretical step which lasts for 4 weeks. The second step is the hands-on step which will last for 2 to 6 months, this is flexible based on the participants' pace and rhythm. Apparently, the faster they work, the earlier the article will be ready.

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