



JOHNS HOPKINS  
BLOOMBERG  
SCHOOL *of* PUBLIC HEALTH

## ***Development of Evidence-Based Preventive Medicine: Probiotics for Diabetes***

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NCDs are all **preventable**

Why do Thai patients still suffer from NCDs that could completely be prevented?

# Scenario of NCDs in Thailand

Increase in prevalence of non-communicable diseases (NCDs) in Thailand

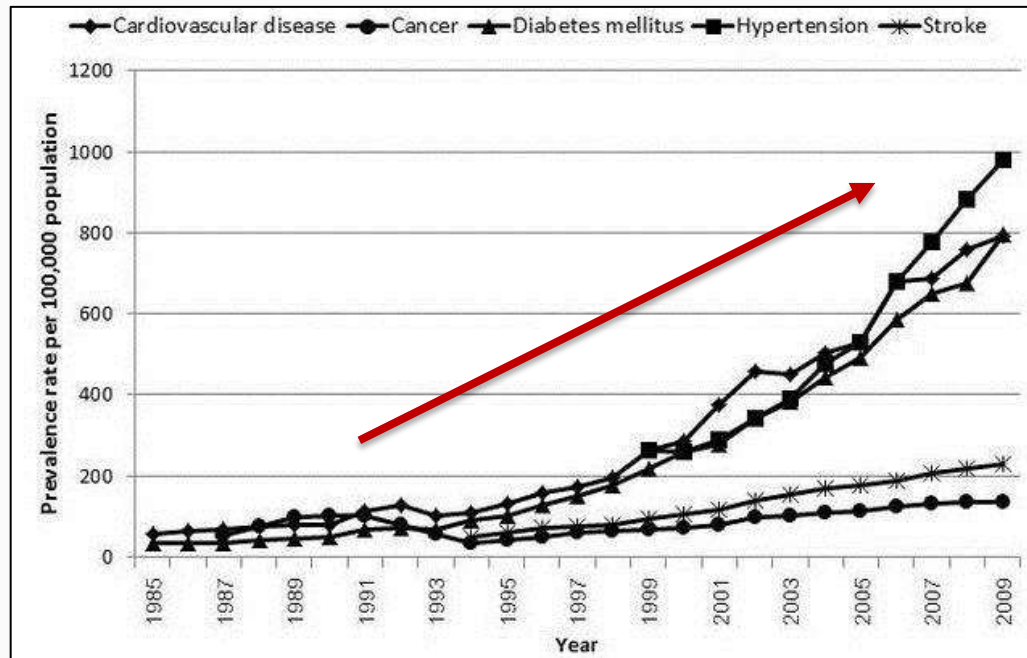
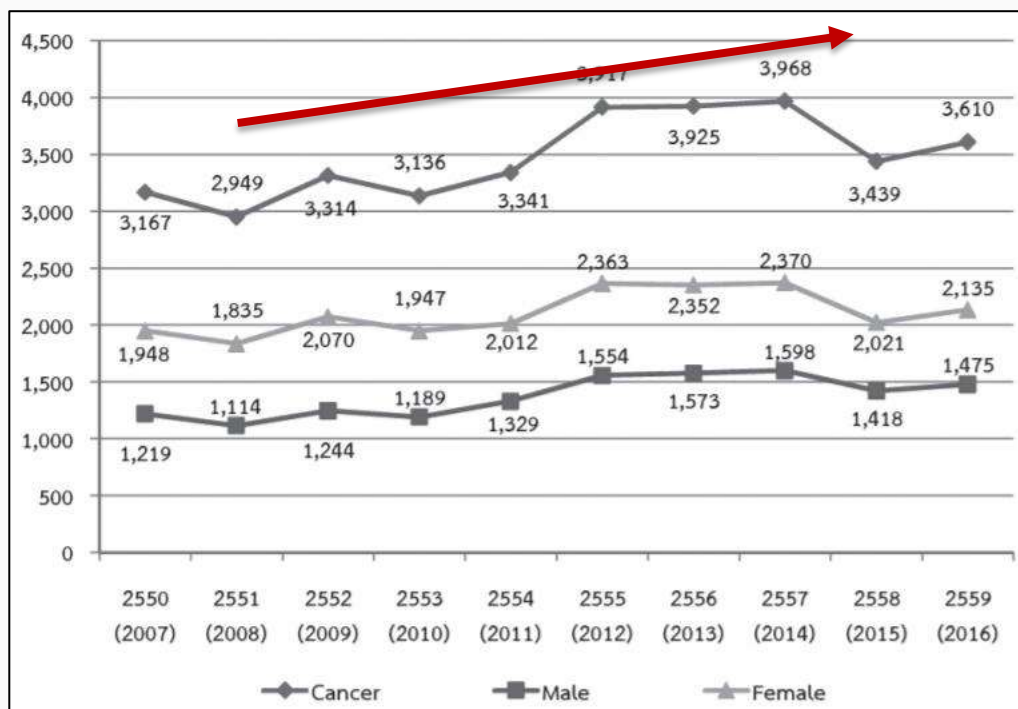


Figure from Chavasit, Visith & Kriengsinyos, Wantanee & Tangsuphoom, Nattapol & Photi, Juntima. (2014). Fast foods in transition and nutrition problems in Thailand.

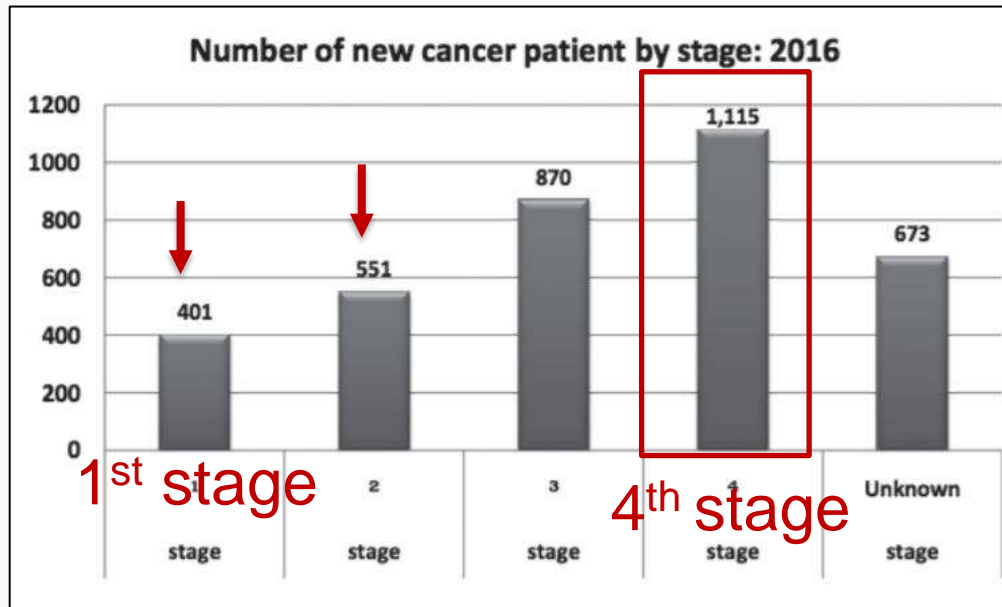
# Scenario of NCDs in Thailand

Trend of number of all new cancer patients by sex: 2007 - 2016



Credit from hospital-based cancer registry annual report 2016

# Scenario of NCDs in Thailand



Credit from hospital-based cancer registry annual report 2016

# What's the missing link?

## Effective Preventive Medicine Recommendation

### Evidence-based

Use evidence from  
high-quality systematic  
review

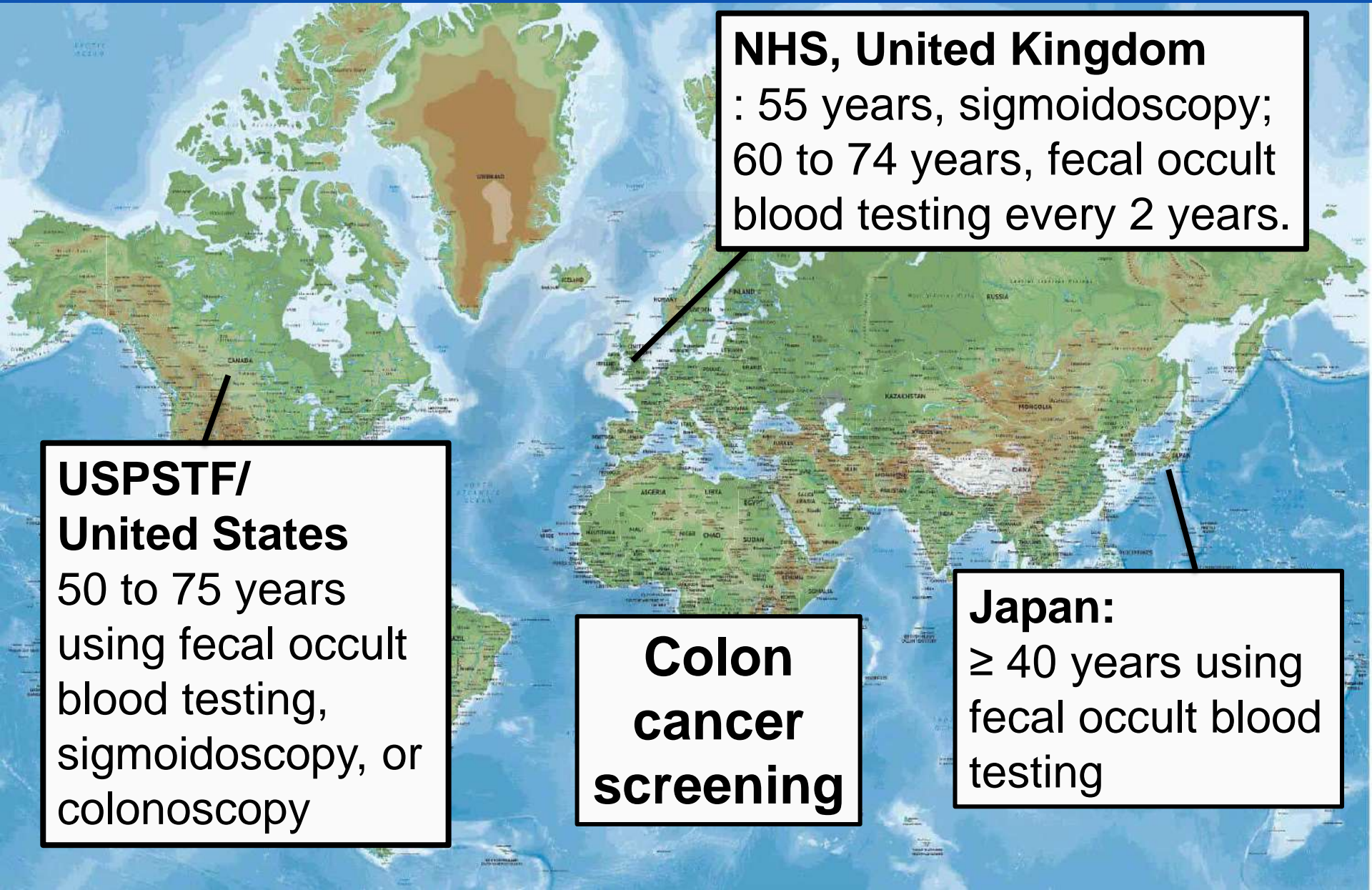


### Context-sensitive

Differences in...

- disease characteristics
- resources' availability
- basic knowledge of related health care providers
- financing mechanism
- clinicians and patients' beliefs and cooperation among countries

# *Scenario of Evidence-based and context-sensitive preventive medicine recommendation*



**NHS, United Kingdom**  
: 55 years, sigmoidoscopy;  
60 to 74 years, fecal occult  
blood testing every 2 years.

**USPSTF/  
United States**  
50 to 75 years  
using fecal occult  
blood testing,  
sigmoidoscopy, or  
colonoscopy

**Colon  
cancer  
screening**

**Japan:**  
≥ 40 years using  
fecal occult blood  
testing



# Development of Evidence-Based Preventive Medicine: Probiotics for Diabetes



Cochrane

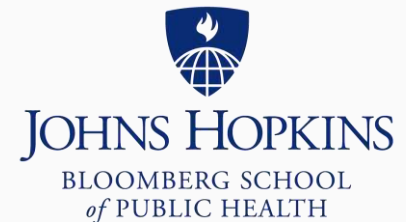


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# Development of Evidence-Based Preventive Medicine: Probiotics for Diabetes

## Project goals

- (1) To identify a context-sensitive topic
- (2) To synthesize evidence through a systematic review for developing evidence-based recommendations.



PROTOCOL

Open Access

## Probiotics for glycemic control in patients with type 2 diabetes mellitus: protocol for a systematic review



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### Abstract

**Background:** Type 2 diabetes mellitus (T2DM) is a major public health problem worldwide. It is characterized by the increased concentration of glucose in the blood and leads to damage of the body system, especially blood vessels and nerves. Lifestyle modification is often combined with anti-diabetic therapy as the standard of care for T2DM to maintain the proper blood glucose and to prevent long-term diabetic complications. The role of probiotics in improving glycemic control has been investigated in several randomized controlled trials (RCTs). Previous systematic reviews and meta-analyses, including different sets of trials have concluded an overall beneficial effect of probiotics in patients with T2DM. At least two RCTs with a longer treatment duration have been published since the publication of existing reviews.

**Methods:** We will conduct a systematic review of RCTs that evaluated the effectiveness and safety of probiotics for glycemic control in T2DM patients. Primary outcomes are fasting blood glucose and glycosylated hemoglobin (A1c). Secondary outcomes are plasma insulin, blood lipid profile, adverse events, and cost associated with the intervention and hospital visits. We will search PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, and trial registries. Two reviewers will independently screen titles and abstracts, review full texts, extract information, and assess the risk of bias. We will summarize the results both qualitatively and statistically. We will use random-effects model for meta-analysis.

**Discussion:** This systematic review aims to examine whether probiotics are effective and safe for glycemic control in T2DM patients. Evidence generated from this review will inform clinical and public health practice and future research.

**Systematic review registration:** CRD42019121682

**Keywords:** Glycemic control, Probiotics, Type 2 diabetes, Systematic review

### Background

#### Description of the condition

Diabetes mellitus is a chronic disease characterized by impaired insulin sensitivity or production, which leads to increased blood glucose concentration and eventually damage to the body system, especially blood vessels and nerves [1]. Type 2 diabetes mellitus (T2DM) is the most

common form of diabetes [2]. The standard treatment of T2DM is lifestyle modification, often combined with anti-diabetic therapy (oral anti-diabetic medication with or without insulin therapy) to maintain the proper blood glucose and to prevent long-term diabetic complications [3].

Patients with poorly controlled blood glucose are at risk for both microvascular complications such as renal, retinal, and neuropathy diseases, as well as macrovascular complications such as peripheral vascular diseases and coronary diseases. These complications lead to morbidity and mortality [2, 4, 5].

Diabetes is a major public health problem. In 2017, it was estimated that 451 million people have diabetes

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# Systematic review methodology at Cochrane

## (1) Identify topic and formulate research question

### Three considerations

#### Condition

highly  
prevalent and  
costly disease



Type 2 diabetes  
mellitus

#### Intervention

context-sensitive



Probiotics usage  
is sensitive to  
ethnicities and  
cultural lifestyles

#### Recent evidence

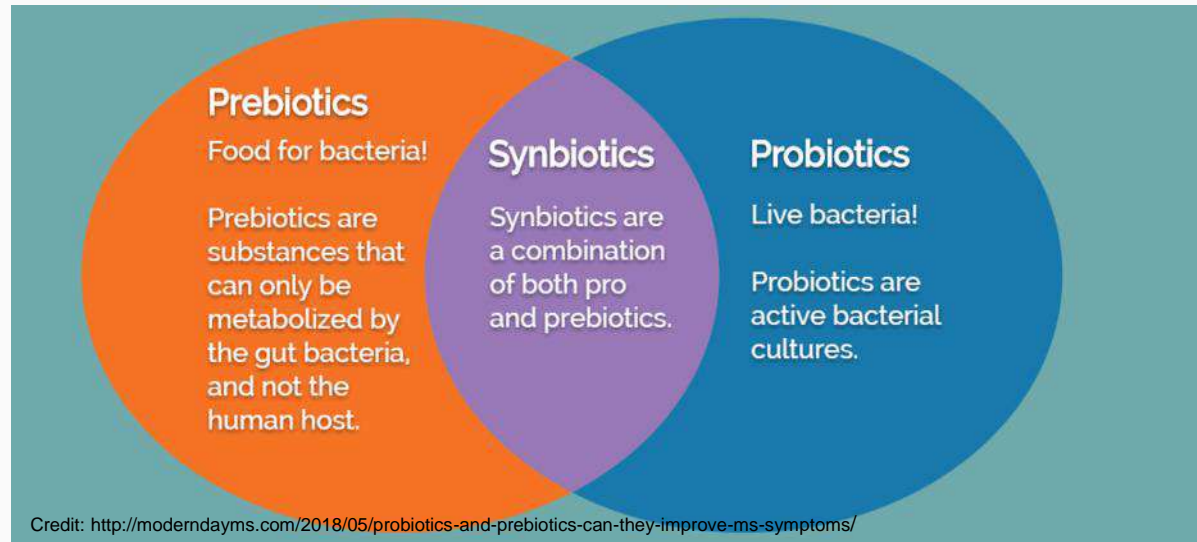
The role of  
probiotics in  
improving glycemic  
control has been  
investigated in  
several randomized  
controlled trials

## **(1) Identify topic and formulate research question**

### **Research question**

Are probiotics effective and safe for glycemic control in patients with type 2 diabetes mellitus?

# What are probiotics?



# What are probiotics?

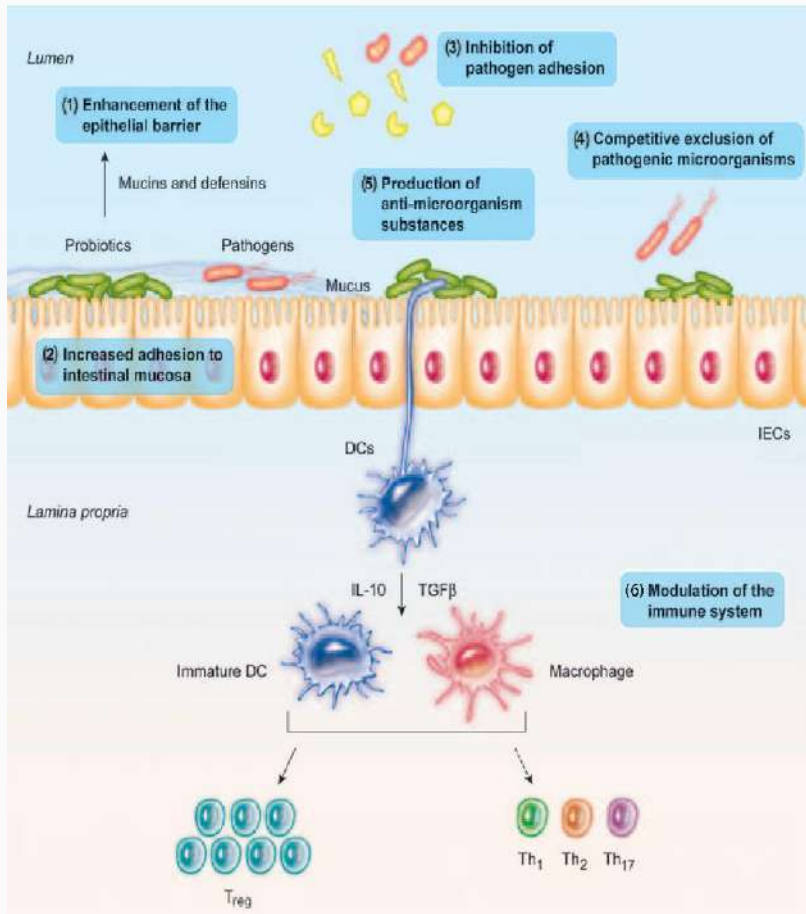
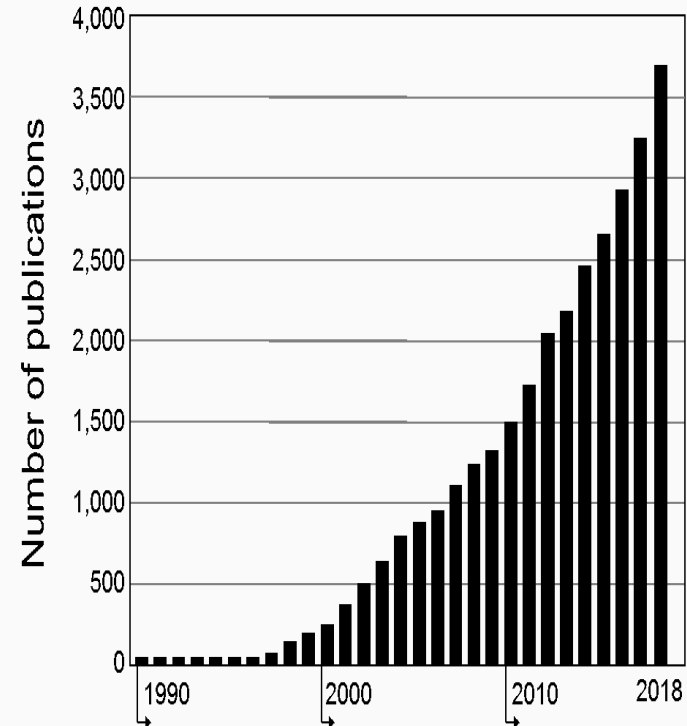


Figure 1 from Bermúdez-Brito, Miriam, Julio Plaza-Díaz, Sergio Muñoz-Quezada, Carolina Gómez-Llorente and Ángel Gil. "Probiotic mechanisms of action." *Annals of nutrition & metabolism* 61 2 (2012): 160-74 .

## Number of scientific publications on probiotics and prebiotics in Pubmed from 1990 to 2018



Scientific publications on probiotics and prebiotics in the PubMed data base, 1990 - 2018. Adapted from Hutkins, 2019.

Credit: ISAPP Science Blog-Reading, writing, and making an impact

## **(2) Synthesize evidence through a systematic review**

### **What systematic review is...**

A systematic review uses robust methods to minimize bias in gathering, summarizing, presenting, interpreting, and reporting research evidence.

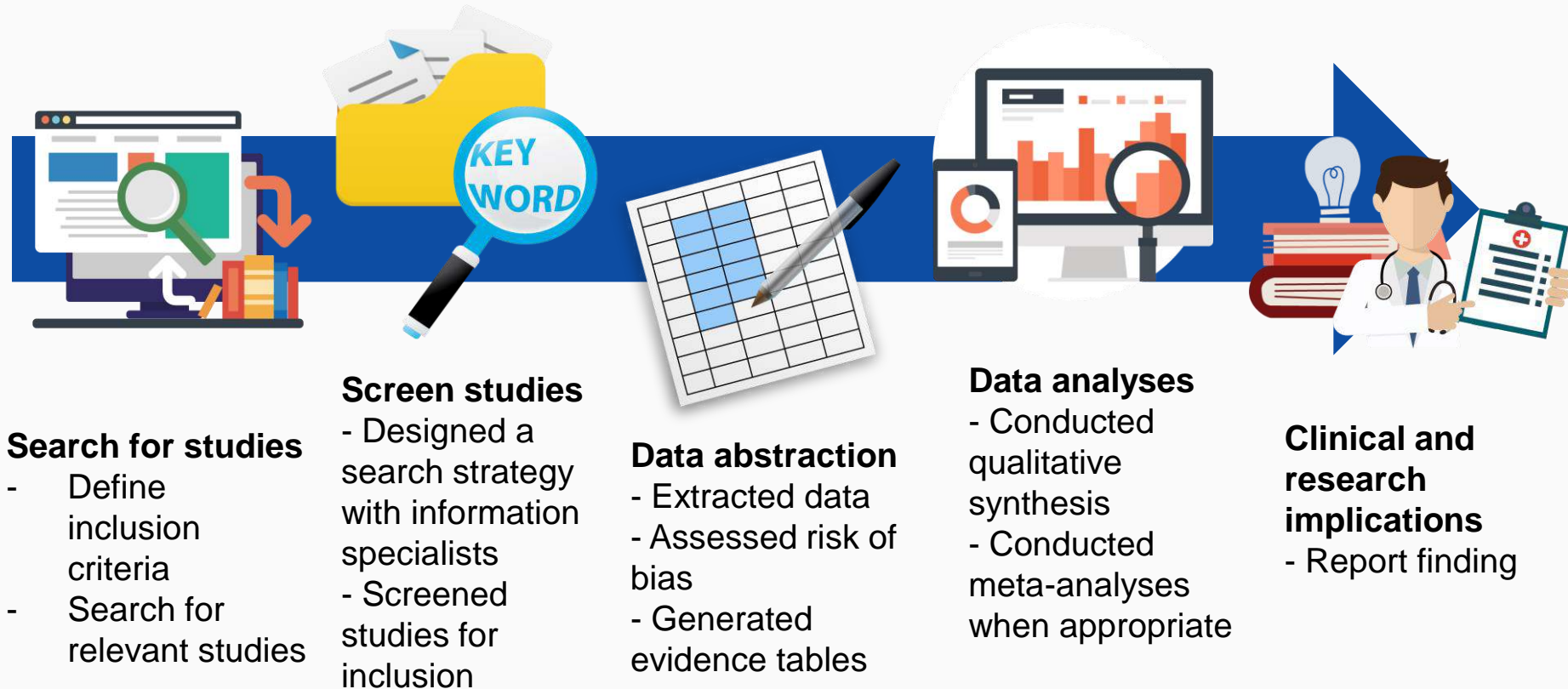
“Systematic reviews aim to provide an up-to-date summary of the state of research knowledge on an intervention, diagnostic test, prognostic factor or other health or healthcare topic.” – Toby J Lasserson, James Thomas, and Julian PT Higgins. Cochrane Handbook, Chapter 1



# Systematic review methodology at Cochrane

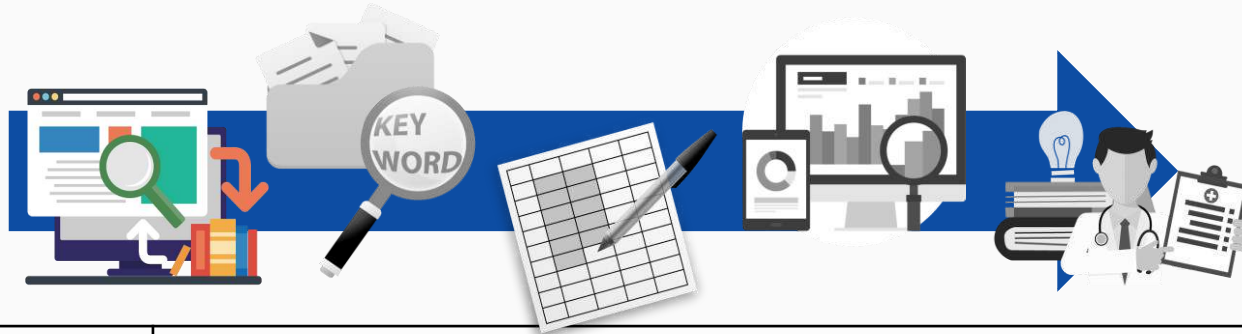
## How to synthesize evidence through systemic review...

### 5 essential steps



# Systematic review methodology at Cochrane

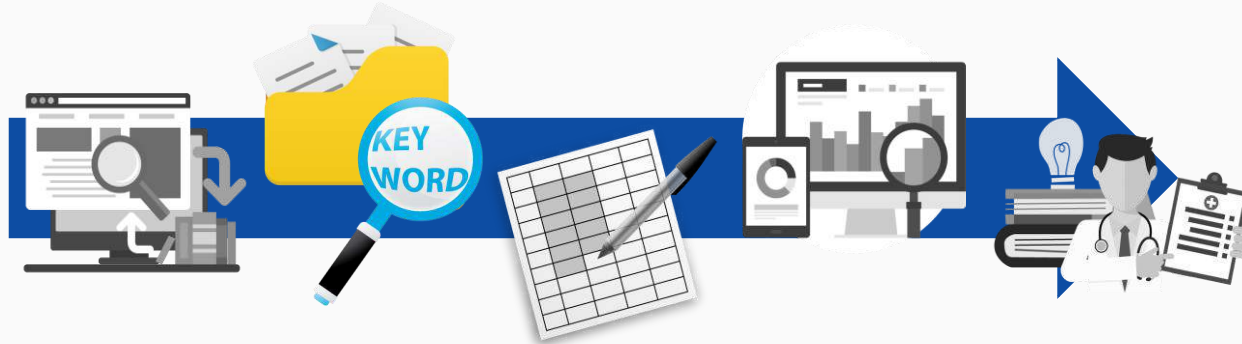
## STEP 1: Define inclusion criteria using PICOTS format



<b><u>P</u>articipants</b>	T2DM or prediabetes patients
<b><u>I</u>ntervention</b>	Probiotics or synbiotics (probiotics + prebiotics)
<b><u>C</u>omparison</b>	Placebo or no intervention; prebiotics (for synbiotics trials)
<b><u>O</u>utcomes</b>	<b>Primary:</b> <ul style="list-style-type: none"><li>• Mean change in fasting blood glucose from baseline</li><li>• Mean change in glycosylated hemoglobin from baseline</li></ul> <b>Secondary:</b> plasma insulin, triglyceride, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), adverse outcomes, health services outcomes
<b><u>T</u>ime points</b>	Short term (<12 weeks) and long term (≥12 weeks)
<b><u>S</u>tudy types</b>	Randomized-controlled trials

# Systematic review methodology at Cochrane

## STEP 2: Screen studies



- Designed a search strategy with information specialists
- Screened abstract/titles and full text independently

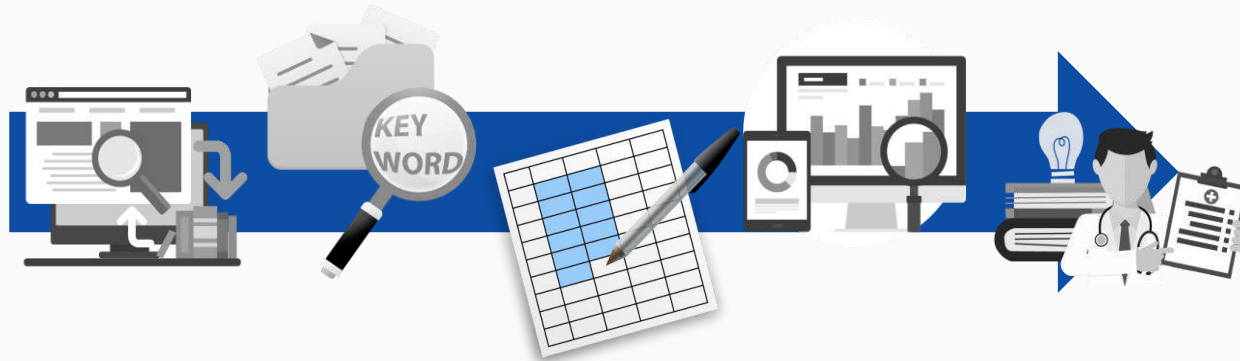
PubMed

Embase<sup>®</sup>



Cochrane

## STEP 3: Data abstraction



- Extracted data
- Assessed risk of bias
- Generated evidence tables

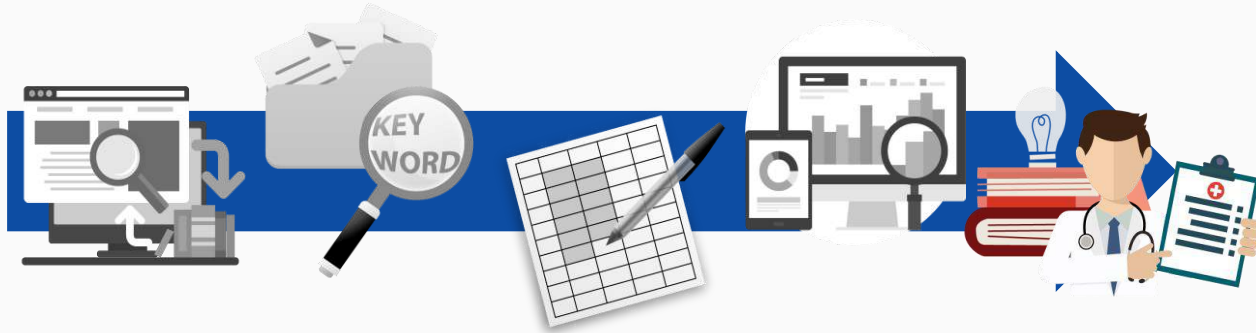
## STEP 4: Data analyses



- Conducted qualitative synthesis
  - Describe: the nature of included studies
  - Interpret: the possible effect of differences among studies
  - Evaluate: the strengths and weaknesses of evidence
  - Conclude: Combinability?
- Conducted meta-analyses when appropriate

# Systematic review methodology at Cochrane

## STEP 5: Clinical and research implications



# Acknowledgment

