

PICO Worksheet and Search Strategy Protocol

1. Defining PICO question by identifying: Patient/Problem (P), Intervention (I), Comparison (C), and Outcome (O):
 - Patient/Problem: **Human colorectal cancer cells**
 - Intervention: **Tocotrienols (α , β , γ , & δ)**
 - Comparison: **Untreated colorectal cancer cells (*if any*)**
 - Outcome: **Modulated genes and proteins**

2. Type of PICO question:
 - Therapy**
 - Prevention**
 - Diagnosis
 - Etiology
 - Prognosis

3. The main topics and alternate terms that can be used for the search:
 - Tocotrienols**
 - Genes**
 - Proteins**
 - Colorectal cancer**
 - Colon cancer**

- ∴ PICO question: What genes and proteins that tocotrienols modulate in colorectal cancer cells to induce anti-cancer effects?

4. Type of studies to include in the search:
 - Research studies or articles**
 - Meta-analysis
 - Systematic review
 - Clinical practice guidelines
 - Randomized controlled trial
 - Case report or series
 - Research report or other grey literature

5. Additional limits that may apply to the search:
 - Year(s) of publication: 2010-2021 (Present)**
 - Language(s): English**
 - Gender: N/A
 - Age: N/A

6. The databases for the search:

- Ovid MEDLINE**
- PubMed**
- Scopus**
- Embase**

7. PICO search strategy:

- Tocotrienol* [Truncated – Stemming]
- **AND** Gene* [Truncated – Stemming] **OR** Protein* [Truncated – Stemming]
- **AND** Colorectal **OR** Colon
- **AND** Cancer

∴ **Table S1.** Inclusion and exclusion criteria for screening and full-text review.

Category	Included	Excluded
Problem type	Human colon cancer cells	Animal colon cancer cells
Intervention type	Tocotrienols (α , β , γ , & δ)	Tocopherols (α , β , γ , & δ)
Outcome type	Modulated genes/proteins	Synergistic effects
Study type	Research studies only	All other types of studies and reviews
Study design	<i>In vitro</i> studies only	<i>In vivo</i> studies and others
Publication Language	English only	Any other languages
Publication period	Published between 2010-2021	Published before 2010