

Meta-Analysis Project Documentation

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1. Input Topic

Topic: Resveratrol supplementation and type 2 diabetes

2. Database Search

Due to missing license I was only using PubMed API.

Search queries generated by LLM:

- ```
(Resveratrol OR trans-Resveratrol OR 3,5,4'-trihydroxystilbene OR stilbene) AND ("Diabetes Mellitus, Type 2" OR T2DM OR "Insulin Resistance" OR hyperglycemia OR "Impaired Glucose Tolerance" OR prediabetes) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
("Resveratrol"[MeSH] AND "Diabetes Mellitus, Type 2"[MeSH]) AND ("Clinical Trial"[Publication Type] OR "Randomized Controlled Trial"[Publication Type] OR "Controlled Study"[Publication Type]) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
(resveratrol[tiab] AND (HbA1c[tiab] OR HOMA-IR[tiab] OR "insulin sensitivity"[tiab] OR "glucose control"[tiab])) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
(Resveratrol AND Supplementation AND (T2DM OR NIDDM OR prediabetes)) AND (Humans[Mesh]) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
(Resveratrol OR SRT501) AND ("Insulin Resistance" OR "Oxidative Stress" OR "SIRT1" OR "Glucose Metabolism") NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
(Resveratrol AND T2DM) AND ("randomized controlled trial"[pt] OR "clinical trial"[pt]) AND (2010:2024[dp]) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```
- ```
("3,5,4'-trihydroxystilbene" OR "Resveratrol formulation") AND (T2DM OR NIDDM) NOT ("systematic review"[Publication Type] OR "meta-analysis"[Publication Type] OR "review"[Publication Type])
```

**Search results:** 281 articles retrieved

## 3. Abstract-Based Pre-filtering

Based on fetched PubMed metadata, articles were pre-filtered using LLM analysis of abstracts.

**GOOD CANDIDATES should have:**

- Clear randomized controlled trial (RCT) or systematic review methodology
- Well-defined study population and intervention
- Measurable primary and secondary outcomes
- Statistical analysis with effect sizes, confidence intervals, or p-values
- Clinical relevance and significance
- Adequate sample size

- Clear inclusion/exclusion criteria

### **BAD CANDIDATES typically have:**

- Case reports or case series (small  $n < 10$ )
- Editorial comments, letters, or opinions
- Animal studies or in vitro studies only
- Lack of control groups
- Unclear methodology or outcomes
- Preliminary or pilot studies without sufficient power
- Studies with major methodological flaws
- Conference abstracts without full methodology

### **Sample abstract-based classifications:**

#### **Example 1 - GOOD CANDIDATE:**

- PMID: 35240291
- Classification: Good Candidate
- Confidence Score: 1.0
- Reasons: "[Clear Randomized Controlled Trial (RCT) methodology (double-blind, placebo-controlled)., 'Well-defined clinical population (T2DM patients) and intervention (Resveratrol 200 mg/day, 24 weeks).', 'Measurable primary and secondary clinical outcomes (glucose, HbA1c, inflammatory markers).', 'Results reported with effect sizes and 95% Confidence Intervals (CIs).', 'Adequate sample size (N=110 recruited).']"

#### **Example 2 - BAD CANDIDATE:**

- PMID: 39317551
- Classification: Bad Candidate
- Confidence Score: 1.0
- Reasons: "[Pre-clinical animal study (Type 2 diabetes rat model)., 'Involves in vitro experimentation (HUVECs).', 'Focuses on molecular mechanisms (ferroptosis, Nrf2).']"

**Result:** 39 articles remained after abstract filtering

## **4. Full-Text Article Download**

As lack of license only publicly available open access articles were downloaded. Download attempted using PubMed API, with fallback to DOI link following.

**Result:** 31 articles successfully downloaded

## **5. Article Classification**

Remaining full-text articles were classified one-by-one using LLM analysis:

### **Classification categories:**

- `article_type`  
: Article type classification
- `candidate_meta_analysis`  
: Suitability for meta-analysis
- `cochrane_bias`  
: Cochrane bias risk assessment

- `data_type`  
: Type of data presented
- `species`  
: Species studied
- `study_type`  
: Study design type
- `clinical_test`  
: Clinical tests/measurements
- `cohort`  
: Cohort characteristics

Each classification includes evidence references from the source text.

## 5.1. Full-Text Classification for Meta-Analysis Candidacy

Based on the full text, each article was evaluated to determine if it contains any "no-go" stop words or criteria that would exclude it from meta-analysis. The LLM assessed each article's candidacy using the

`candidate_meta_analysis`

classifier.

### Classification criteria:

- Articles with clear methodology, control groups, and quantifiable outcomes are marked as CANDIDATE
- Articles with case reports, editorials, reviews without original data, or methodological flaws are marked as NOTACANDIDATE
- Confidence levels (High, Medium, Low) indicate the certainty of the classification

### Sample classifications:

#### Example 1 - CANDIDATE (High Confidence):

- PMID: 35240291
- Classification: CANDIDATE
- Confidence: High
- Assessment: "The study is a randomized, placebo-controlled trial that meets all primary assessment criteria. It compares an intervention (resveratrol) against a control (placebo) in a defined population (T2DM patients) and reports sufficient quantitative data, including mean changes, standard errors, and mean differences with 95% confidence intervals, for key continuous outcomes. Therefore, it is highly suitable for inclusion in a quantitative meta-analysis."

#### Example 2 - NOTACANDIDATE:

- PMID: 34371884
- Classification: NOTACANDIDATE
- Confidence: High
- Assessment: "The study is based on a robust randomized, controlled design with clear PICO elements. However, the specific content of this published article is focused on secondary correlation analyses of the trial data. It fails to provide the basic comparative summary statistics (Means and SDs for both arms at endpoint) necessary for direct calculation of effect sizes, thus precluding its use as a stand-alone candidate for quantitative meta-analysis."

**Result:** 23 articles confirmed as candidates for meta-analysis after full-text review

## 5.2. Full-Text Classification for Study Type

Based on the full text, each article was evaluated to determine if it contains any "no-go" stop words or criteria that would exclude it from meta-analysis. The LLM performed study type classification to categorize the research design.

### Study type classifications:

- Randomized Controlled Trial (RCT)
- Cohort Study
- Case-Control Study

### Sample study\_type classifier results:

#### Example 1 - study\_type classifier result:

- PMID: 35240291
- Classification: "Randomized Controlled Trial"
- Confidence: "High"
- Evidence: "This study is explicitly identified in the title, abstract, and Section 2.1 as a "randomized, double blinded placebo-controlled parallel group trial." Participants were selected (n=110) and then subjected to a random allocation process, assigning them to either the intervention group (resveratrol 200 mg/day) or the control group (placebo/cellulose capsules). The study then followed these groups prospectively for 24 weeks to assess the primary and secondary outcomes (e.g., FPG, HbA1c, HOMA-IR, inflammatory markers). The presence of random assignment to intervention groups meets the definitive criterion for a Randomized Controlled Trial (RCT)."

#### Example 2 - study\_type classifier result:

- PMID: 32900519
- Classification: "Randomized Controlled Trial"
- Confidence: "High"
- Evidence: "The study is explicitly identified in the title and the methods section (Section 2.1) as a '24-month randomised, double-blind, placebo-controlled, two-period crossover intervention trial.' Participants were allocated to either the active intervention (resveratrol) or the control (placebo) using a random assignment mechanism ('Altman's randomisation by minimisation procedure,' Section 2.5). The study design involves an experimental intervention (supplementation) and prospective outcome measurement over 24 months, satisfying all criteria for a Randomized Controlled Trial."

## 6. Meta-Analysis Target Selection

Based on available cohorts and clinical tests, LLM analysis identified: *"The most suitable clinical test for meta-analysis — one that provides the strongest evidence base and the widest coverage across studies."*

Due to limited time and resources, only 1 meta-analysis target was selected.

### Selected target:

```
json
{
 "selectedclinicaltest": "Glycated Hemoglobin (HbA1c)",
 "justification": "HbA1c is a standardized, clinically vital marker for long-term glycemic
```

```
control, frequently reported across the studies, especially those involving Type 2 Diabetes. Its
stability and relevance make it an excellent primary outcome for meta-analysis, superior to more
volatile measures like fasting glucose.",
"recommended cohorts": [
 "Patients with Type 2 Diabetes (Resveratrol Intervention)",
 "Patients with Type 2 Diabetes (Placebo Control)",
 "Overweight/Obese Individuals with Metabolic Dysfunction"
]
}
```

## 7. Data Point Extraction

Based on the suggested meta-analysis target, all PDFs were processed individually to extract relevant data using multimodal Pro LLM.

**Sample extracted datapoints:**

```
studyid authoryear country populationtype samplesizeintervention samplesizecontrol
interventionname dosemgperday durationdays outcomename biomarkerunit interventionbaselinemean
interventionbaselinesd interventionpostmean interventionpostsd controlbaselinemean
controlbaselinesd controlpostmean controlpostsd meandifference sddifference pvalue
effectdirection statisticalsignificance
35240291 Mahjabeen2022 Pakistan Type2Diabetes 55
55 Resveratrol 200.0 168 HbA1c 55
percent 8.64 1.34
8.2 8.4 1.15
8.42 NaN -0.45 NaN 0.033
decrease yes
30237505 Bo2018 Italy Type2Diabetes 65
62 Resveratrol 500.0 180 HbA1c 65
percent 6.90 1.20
NaN NaN 6.9 1.00
NaN NaN NaN NaN
NaN NaN NaN
30237505 Bo2018 Italy Type2_Diabetes 65
62 Resveratrol 40.0 180 HbA1c 65
percent 7.20 1.30
NaN NaN 6.9 1.00
NaN NaN NaN NaN
NaN NaN NaN
```

## 8. Meta-Analysis Execution

LLM generated Python code to create Forest plots and statistical tables for the meta-analysis.

## 9. Cochrane Bias Risk Assessment

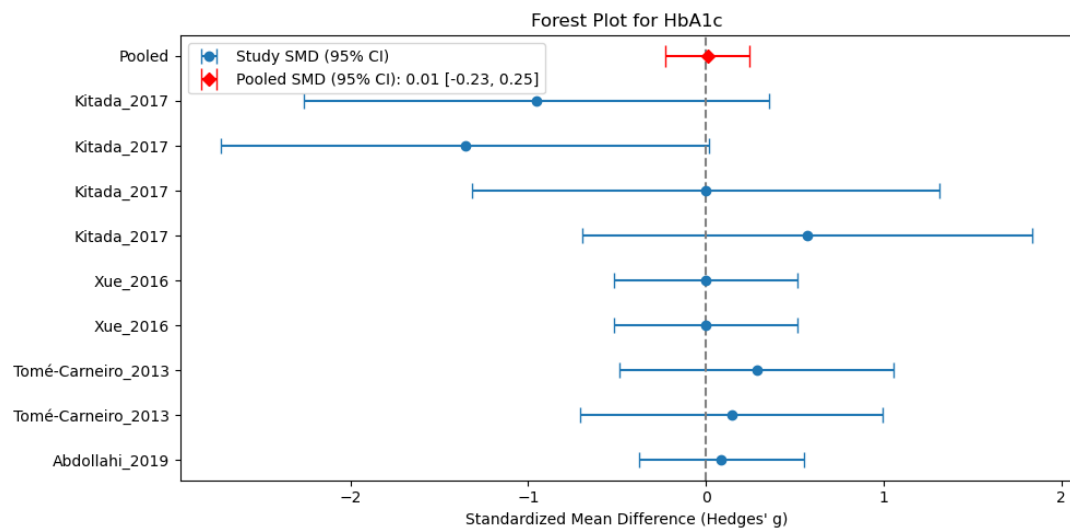
| PMID     | Author Year         | Randomization | Deviations | Missing Data | Measurement | Selection |
|----------|---------------------|---------------|------------|--------------|-------------|-----------|
| 35240291 | Mahjabeen_2022      | False         | False      | False        | False       | False     |
| 30237505 | Bo_2018             | False         | False      | True         | False       | False     |
| 29914666 | Khodabandehloo_2018 | False         | False      | True         | False       | False     |
| 29357033 | Seyyedebrahimi_2018 | False         | False      | False        | False       | False     |
| 32144833 | Tabatabaie_2020     | False         | False      | False        | False       | False     |
| 27520400 | Bo_2016             | False         | False      | False        | False       | False     |
| 31475415 | Abdollahi_2019      | False         | True       | False        | False       | False     |
| 23557933 | Tomé-Carneiro_2013  | True          | False      | False        | False       | False     |
| 27207552 | Xue_2016            | True          | False      | False        | False       | True      |

| PMID     | Author Year | Randomization | Deviations | Missing Data | Measurement | Selection |
|----------|-------------|---------------|------------|--------------|-------------|-----------|
| 29057795 | Kitada_2017 | True          | False      | True         | False       | False     |

## 10. Results

**Topic:** Resveratrol supplementation and type 2 diabetes

**Generated visualizations:**



## Statistical Results:

```
Successfully loaded 17 rows from extracteddatapoints.csv
Columns: ['studyid', 'authoryear', 'country', 'populationtype', 'samplesizeintervention',
'samplesizecontrol', 'interventionname', 'dosemgperday', 'durationdays', 'outcomename',
'biomarkerunit', 'interventionbaselinemean', 'interventionbaselinesd', 'interventionpostmean',
'interventionpostsd', 'controlbaselinemean', 'controlbaselinesd', 'controlpostmean',
'controlpostsd', 'meandifference', 'sddifference', 'pvalue', 'effectdirection',
'statisticalsignificance']
Outcomes available: ['HbA1c']
Studies: ['Mahjabeen2022' 'Bo2018' 'Khodabandehloo2018' 'Seyyedebrahimi2018'
'Tabatabaie2020' 'Bo2016' 'Abdollahi2019' 'Tomé-Carneiro2013'
'Xue2016' 'Kitada2017']
```

```
After cleaning missing values: 9 rows remaining
Outcomes with multiple studies: ['HbA1c']
```

### GENERATED CHARTS

```
--- Meta-analysis for HbA1c ---
```

|    | authoryear        | interventionname       | dosemgperday | g         | seg      |
|----|-------------------|------------------------|--------------|-----------|----------|
| 8  | Abdollahi2019     | Resveratrol            | 1000.00      | 0.087130  | 0.237492 |
| 9  | Tomé-Carneiro2013 | Resveratrol            | 12.15        | 0.145445  | 0.434183 |
| 10 | Tomé-Carneiro2013 | Resveratrol            | 12.15        | 0.285185  | 0.394221 |
| 11 | Xue2016           | Resveratrol+Hesperetin | 90.00        | 0.000000  | 0.262613 |
| 12 | Xue2016           | Resveratrol+Hesperetin | 90.00        | 0.000000  | 0.262613 |
| 13 | Kitada2017        | Piceatannol            | 20.00        | 0.571250  | 0.645226 |
| 14 | Kitada2017        | Piceatannol            | 20.00        | 0.000000  | 0.670820 |
| 15 | Kitada2017        | Piceatannol            | 20.00        | -1.354839 | 0.701270 |
| 16 | Kitada2017        | Piceatannol            | 20.00        | -0.952084 | 0.667325 |

```
Pooled SMD (Hedges' g): 0.009
Standard Error of Pooled SMD: 0.122
95% CI: [-0.229, 0.248]
```

Chart: Forest Plot - HbA1c

Filename: metaanalysisforestHbA1c.png

Description: Forest plot showing standardized mean differences for HbA1c with 95% confidence

intervals

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