Meta-Analysis Project Documentation

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1. Input Topic

Topic: Resveratrol supplementation and type 2 diabetes: a systematic review and meta-analysis

2. Database Search

Due to missing license I was only using PubMed API.

Search queries generated by LLM:

1. `(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])`
2. `("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])`
3. `(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])`
4. `(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])`
5. `(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])`
6. `(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])`
7. `("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

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.

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
percent                        8.64                      1.34
8.2                  NaN                    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
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
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.

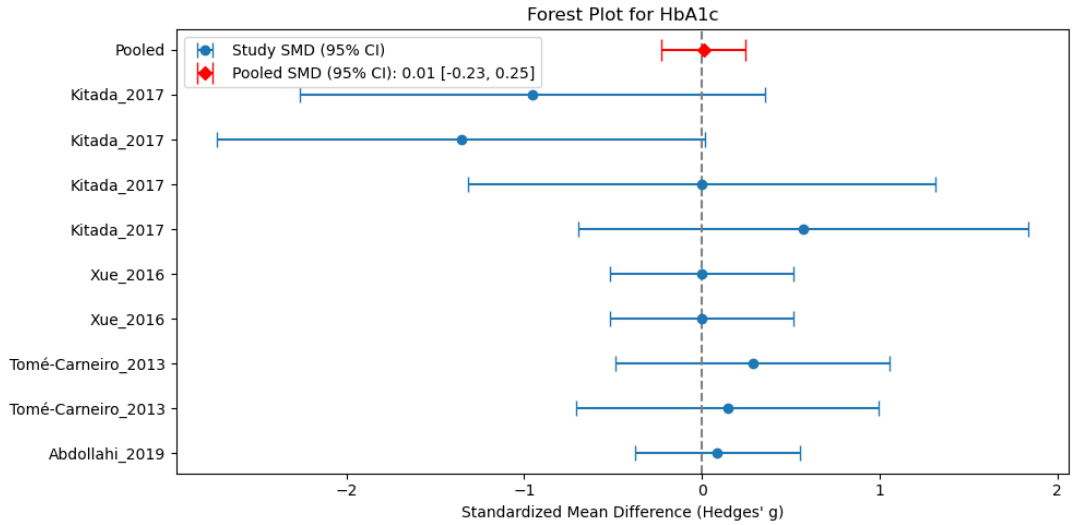
9. Cochrane Bias Risk Assessment

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
29057795	Kitada_2017	True	False	True	False	False

10. Results

Topic: Resveratrol supplementation and type 2 diabetes: a systematic review and meta-analysis

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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```