

A Living Interactive Evidence Synthesis Framework and Applications for Creating and Maintaining Living Systematic Reviews and Meta-Analysis

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Introduction

Systematic Reviews (SRs) and meta-analyses (MAs) are tools to synthesize evidence and provide precise estimates of effects for benefits and harms outcomes with associated certainty of evidence.

However, when the research field rapidly evolves, it requires frequent labor-intensive updates to keep pace with new evidence to keep the systematic reviews and meta-analyses “living” (SRMAs). For truly living SRMAs, several laborious steps still must be done by researchers manually, such as data collection, study screening, and information extraction. Thus, a system that facilitates the steps in SRMA is urgently needed to reduce the time and effort spent on repetitive tasks.

To address this need, we propose a living interactive evidence synthesis (LIV-E) framework that integrates open-source web techniques and MA libraries to maintain living and interactive SRMA.

Study Screener

Study screener can help researchers to screening studies based on inclusion/exclusion criteria.

Data Sources: OVID / Embase / PubMed / Others

Toxicity of Immune Checkpoint Inhibitors 3 Screener Overview

All References

Unscreened (442) 1 **Decided** (8702) 224

Reference List | Unscreened References [Inclusion/Exclusion Criteria](#)

Filters: RCT UNKNOWN RCT Check Later

Sort by: Decision Reason, Decision Date

Tag Filters: [Reset](#) Efficacy MA Toxicity MA E&T MA Biomarkers MA Other MA IO in Control Arm Positive Trial QoL Trial

CEA Etc Phase 2 Phase 3 NA MI SAAN Duplicate

Further Check

Full Text Review (39) 19 Show 10 entries Search:

#	Date	Labels	Title	
9153	PMID: 36914193 2023-03-20	NOT RCT	Neoadjuvant Arterial Embolization Chemotherapy Combined PD-1 Inhibitor for Locally Advanced Rectal Cancer (NECI Study): a protocol for a phase II study.	Exclude By Title
9152	PMID: 36898078 2023-03-20	NOT RCT	Phase II Clinical Trial of Axitinib and Avelumab in Patients With Recurrent/Metastatic Adenoid Cystic Carcinoma.	Exclude By Title
9151	PMID: 36906715 2023-03-20	NOT RCT	Immune priming with avelumab and rituximab prior to R-CHOP in diffuse large B-cell lymphoma: the phase II AvR-CHOP study.	Exclude By Title
9149	PMID: 36916728 2023-03-20	RCT NOT RCT	Pembrolizumab plus chemotherapy in Japanese patients with triple-negative breast cancer: Results from KEYNOTE-355.	Exclude By Title
9148	NCT02239900 PMID: 36921766 2023-03-20	NOT RCT	Five-Year Overall Survival with Ipilimumab and Stereotactic Ablative Radiotherapy for Metastatic Disease.	Exclude By Title
9147	PMID: 36925073 2023-03-20	NOT RCT	Neoadjuvant osimertinib followed by sequential definitive radiotherapy and/or surgery in stage III EGFR-mutant NSCLC: An open-label, single-arm, phase II study.	Exclude By Title
9144	NCT03158129 PMID: 36928818 2023-03-20	NOT RCT	Neoadjuvant chemotherapy plus nivolumab with or without ipilimumab in operable non-small cell lung cancer: the phase 2 platform NEOSTAR trial.	Exclude By Title
9143	PMID: 36928921 2023-03-20	NOT RCT	A Phase II Trial of Guadecitabine plus Atezolizumab in Metastatic Urothelial Carcinoma Progressing after Initial Immune Checkpoint Inhibitor Therapy.	Exclude By Title
9142	NCT04341181 2021717549 2023-03-13	NOT-RCT	ProTarget: a Danish Nationwide Clinical Trial on Targeted Cancer Treatment based on genomic profiling - a national, phase 2, prospective, multi-drug, non-randomized, open-label basket trial.	Exclude By Title
9141	2021799611 2023-03-13	NOT-RCT	Adjuvant Overall Su	

Showing 21 to 30 of 442 entries

Included References

Included (391) 210 13

- Toxicity of Im... (209) 182
- Redundancy ... (134) 257
- All ICI trials (243) 148

Excluded References

By Title (5394) 12 3

By Abstract (2233) 2 5

By Full Text (684) 0 14

Screener Tools

[Update Original/Followup](#)

[Export Reference List](#)

[Show PRISMA](#)

Keywords will be highlighted to help identify relevant studies

After screening, the included studies will be further sent to next step to extract information such as treatment, control, cohort characteristics, etc.

Data Extractor

Data extractor can facilitate the information extraction from full-text PDF files of each paper.

Toxicity of Immune Checkpoint Inhibitors 3 Toxicity of Immune Checkpoint Inhibitors 3 Extract by paper

209 studies (included in SR) PMID, short #, first author name Abstract PDFs

Rossevold A.H. et al 2022
is selected in 74 outcomes

itable
default | Interactive Table

Save 2

- Constitutional
Alopecia
Chills
Decreased appetite
Fatigue
Fever
Malaise
Nausea
Pain
Weight loss

- Electrolyte abnormalities
Hyperkalemia
Hypokalemia
Hypophosphatemia

- Endocrine
Hyperglycemia
Hyperthyroidism
Hypothyroidism

- Gastrointestinal
Abdominal pain
Constipation
Diarrhea
Dysgeusia
Dyspepsia
Dysphagia
Flatulence
Gastroenteritis
Oral dysaesthesia
Oral fungal infection
Pancreatitis
Vomiting

- Hematologic
Anemia
Decreased lymphocyte count
Decreased neutrophil count
Leukopenia

Comp 1

TRIAL CHARACTERISTICS

Study name: ALICE
Trial phase: Phase 2
Number of arms: 2
Original publication or Follow-up: Original publication
Cancer type: Triple negative breast cancer
Treatment regimen: Atezolizumab + Chemotherapy
Name of ICI: Atezolizumab
Class of ICI: PD-L1
Monotherapy/combination: Combination
Type of combination: ICI + Chemotherapy
Control regimen: Placebo + Chemotherapy
Type of control: Placebo+Chemo

POPULATION CHARACTERISTICS

Total sample size: 70
Lines of treatment: Only 1st line of treatment f
Clinical setting in relation to surgery: NA

Atezolizumab plus anthracycline-based chemotherapy in metastatic triple-negative breast cancer: the randomized, double-blind, phase 2b ALICE trial

nature medicine

Article

<https://doi.org/10.1038/s41591-022-01970-w>

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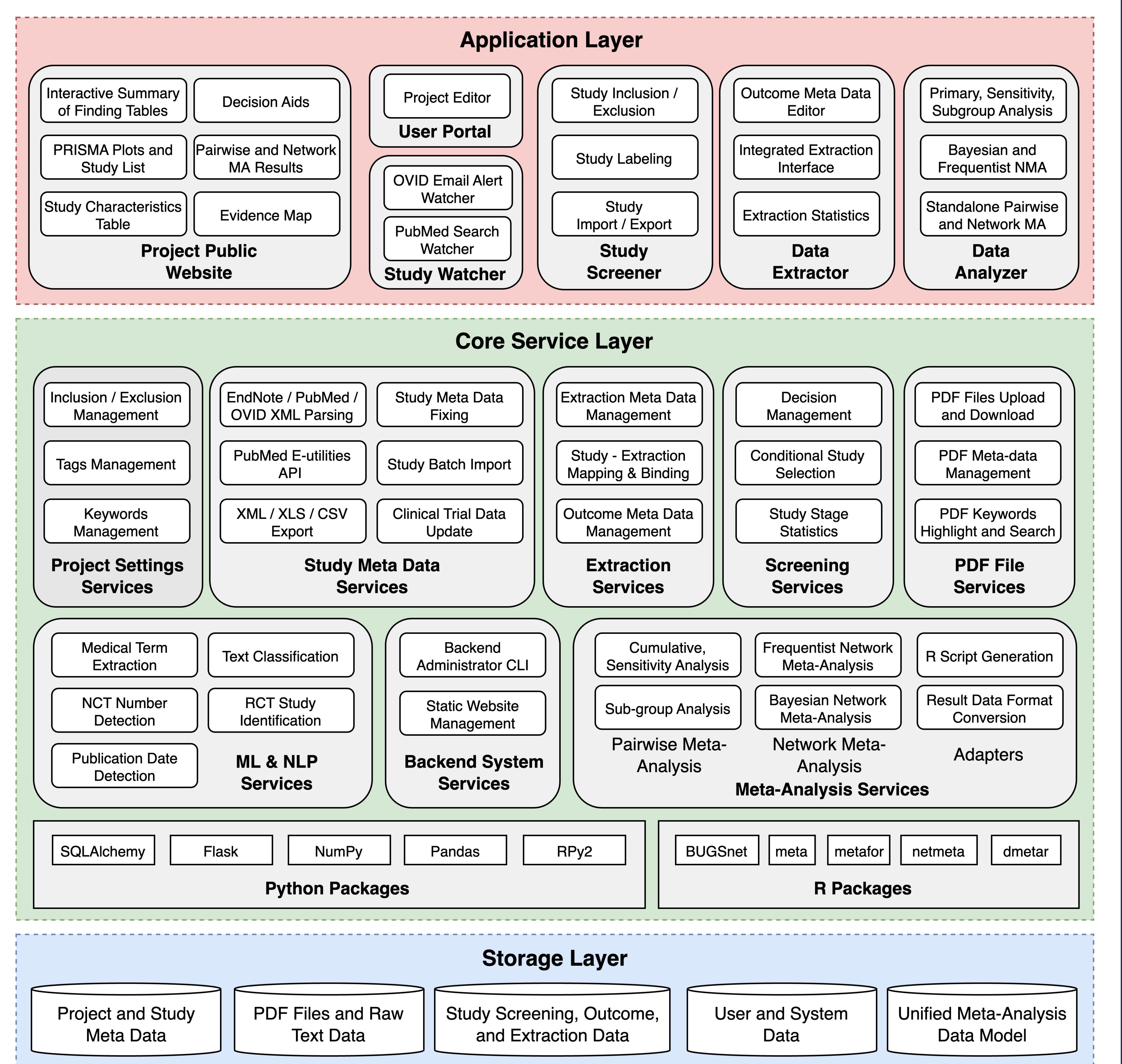
A list of authors and their affiliations appears at the end of the paper

Immune checkpoint inhibitors have shown efficacy against metastatic triple-negative breast cancer (mTNBC) but only for PD-L1^{positive} disease. The randomized, placebo-controlled ALICE trial (NCT03164993, 24 months) evaluated the addition of atezolizumab (anti-PD-L1) to immune-checkpoint inhibitor therapy in mTNBC. Patients received pegylated liposomal doxorubicin (PLD) and low-dose cyclophosphamide in combination with atezolizumab (atezo-chemo; $n = 40$) or placebo (placebo-chemo; $n = 28$). Primary endpoints were descriptive assessment of progression-free survival (PFS) in the per-protocol population (>3 atezolizumab and >2 PLD doses) and safety in the full analysis set (FAS; all patients starting therapy). Adverse events leading to drug discontinuation occurred in 18% of patients in the ateo-chemo arm (7/40) and in 7% of patients in the placebo-chemo arm (2/28). Improvement in progression-free survival was indicated in the ateo-chemo arm in the per-protocol population (median 4.3 months vs. 3.5 months; hazard ratio (HR) = 0.57; 95% confidence interval (CI) log-rank $P = 0.047$) and in the FAS (HR = 0.56; 95% CI 0.33–0.95; $P = 0.03$). A numerical advantage was observed for both the PD-L1^{positive} ($n = 20$; HR = 0.65; 95% CI 0.27–1.54) and PD-L1^{negative} subgroups ($n = 31$; HR = 0.55; 95% CI 0.27–1.21). The progression-free proportion after 15 months was 44.7% (5/11; 95% CI 14.7–74.7%) in the ateo-chemo arm versus 30.1% (9/30; 95% CI 14.7–45.4%) in the placebo-chemo arm. The addition of atezolizumab to PLD/cyclo-

System Architecture

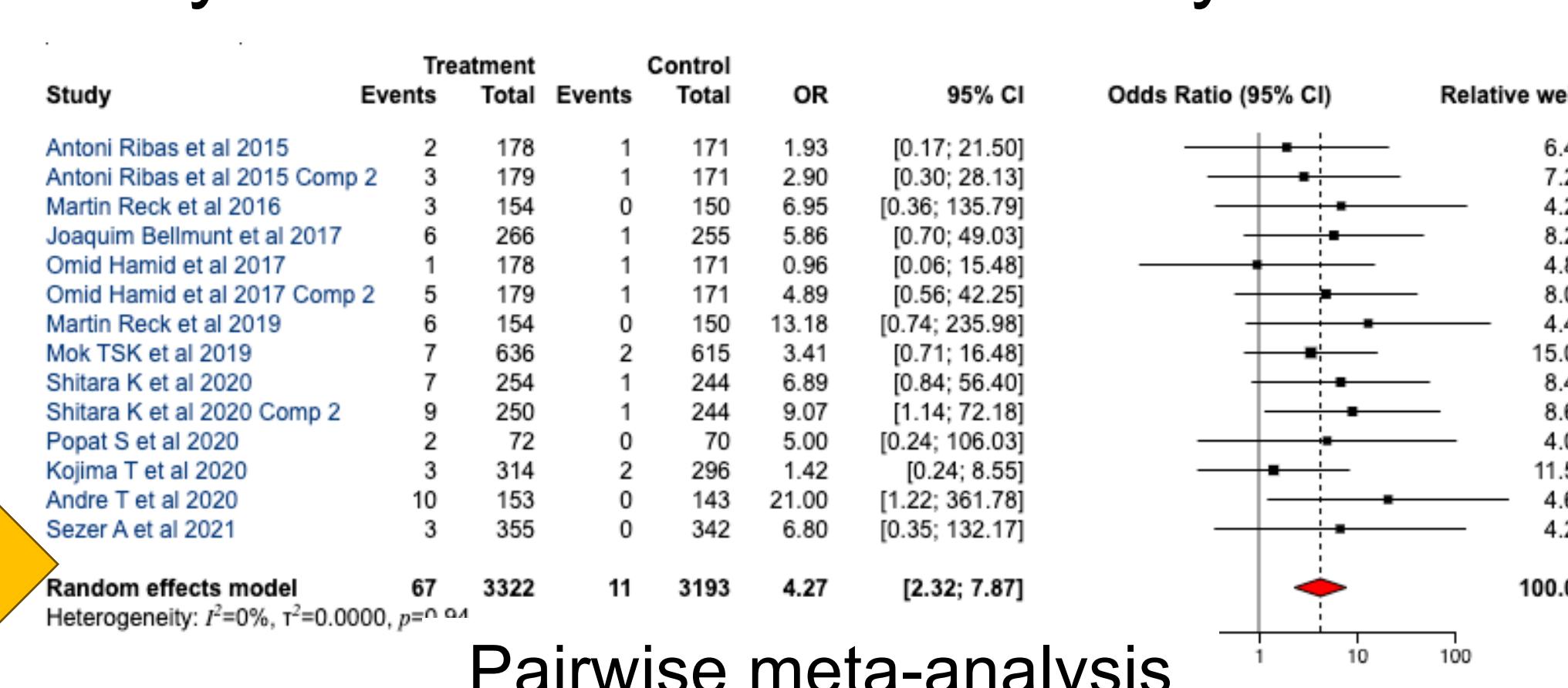
As shown in the following figure, we designed a multi-layer architecture to implement the functions needed by the living SRMA, including:

- 1) **application layer**, which provides the user interface for researchers to screen studies, extract information from selected studies, and conduct MAs to understand the benefits and harms of treatments.
 - 2) **core service layer**, which implements the functionalities needed for conducting the tasks of SRMA, such as project data management, screening decision management, extraction management, and meta-analyses.
 - 3) **storage layer**, which saves all the data generated in the living SRMA process.



Data Analyzer and Public Websites

The extracted data will be sent to data analyzer for conducting pairwise meta-analysis and network meta-analysis.



The screening results, extracted information, and the final meta-analysis results are exported as plots and summary of finding tables in the project public website for public access and exploration.

