

# Demo Walkthrough: Tanezumab for Osteoarthritis

Welcome to the walkthrough of the *Osteoarthritis: Tanezumab* demo Nest (open in your original tab). In this walkthrough, we'll explain the core functionalities of Nested Knowledge through this Nest. We encourage you to work through the Nest as you follow the walkthrough. The Nest available to you is a copy of the original and may be freely modified, so roll up your sleeves and get your hands dirty!

This Nest is a copy of a previously-completed review presenting the evidence regarding the safety and efficacy of tanezumab at different dosage levels for the treatment of osteoarthritis.

## Nest Home

INESTED

KNOWLEDGE

Home: Osteoarthritis: Tanezumab

Nest Home

Dashboard

Literature Search

2/2

Other Sources

Duplicate Review

Search Exploration

Query Builder

Screening

10/201

Configure Exclusion Reasons

Study Inspector

Tagging

30/30

Configure Study Tags

Study Inspector

Extraction

30/30

Study Inspector

Synthesis

Manuscript Editor

Expert

Settings

Admin

Show Table of Contents

ProtocolDescriptionMaterials

About

This Nest is a copy of a previously-completed review presenting the evidence regarding the safety and efficacy of tanezumab at different dosage levels for the treatment of osteoarthritis.

In this nest, you can examine the search, screening, tagging, and extraction completed in this review, as well as editing the protocol (below) and practicing adding and running searches, including and excluding records, editing the tagging hierarchy, and collecting tags and data based on underlying included studies. To follow a guided walk-through of this demo, please visit our [documentation](#).

If you have any questions, view page-specific documentation using the "i" in the upper right, or [contact support](#). Happy nest building!

Review Title:

Safety and efficacy of tanezumab for treatment of chronic pain in patients with osteoarthritis of the hip or knee: A report from a living systematic review and network meta-analysis through Nested Knowledge

Authors:

| Author Name         | Author Role   | Author Affiliation |
|---------------------|---|--------------------|
| Nicole Hardy        | Did 50% of the nest overall. Did ROB adjudication. General project management. Edits to manuscript. | NK                 |
| Mohamed Abdelmegeed | Wrote the manuscript  | SHNE               |
| John Pedersen       | Performed meta-analysis   | SHNE/NK            |
| Kevin Holmes        | Provided general guidance on project.   | NK                 |
| Bernadette Kane     | Did 25% of nest.  | NK                 |
| Azad Rahmatullah    | Did 25% of nest and tables  | NK                 |
| Kathryn Cowie       | Did some tables   | NK                 |
| Kristen Hutchinson  | Did ROB   | NK                 |
| Ranika Tanchand     | Did ROB   | NK                 |

Comments

NextYour MentionsAll Mentions

Mohamed Abdelmegeed

2/10/23, 12:49 PM

@Kevin Holmes

Kevin, based on the paragraph below (in the introduction now in the draft), do you think it may be worth it to do sub analysis for studies 5 mg and below only?

Also it seems that analysis of rapidly progressive OA (RPROA) and osteonecrosis are the most 2 important side effects.

Or

We just include all doses combined?

Tanezumab, monoclonal NGF antibodies, has completed pivotal phase III clinical trials ([PMID:30265100](#); [32234](#)) and is expected to be approved for the treatment of chronic pain in patients with OA or chronic low back pain clinical use soon. Hochberg, 2005 noted that anti-NGF treatment may lead to treatment-related rapidly progressive OA (RPROA) and osteonecrosis, ([PMID:15527256](#)), and that Tanezumab combined with NSAIDs treatment appeared to increase the risk of RPROA, relative to Tanezumab monotherapy. ([PMID:26554876](#)). A partial clinical held by the FDA to assess the results of previous trials, and it was determined that there was a dose-response relationship between osteonecrosis and Tanezumab (dose range, 2.5-10 mg ([PMID:2655448](#); [28779540](#); [31207163](#))). The maximum dose of Tanezumab was reduced from 10 mg to 5mg after [post-market surveillance](#) and [FDA](#) [action](#).

B

/

U

≡

⌕

Comment

You've landed on your demo Nest in AutoLit, and you're looking at the Nest Home page. This page includes a menu on the left of the page, the protocol in the center, and discussion about the Nest on the right. The menu includes links to all modules & configurations available to you in AutoLit. We'll now walk through these modules one by one. (click the title in the menu to navigate to the the corresponding module).

## Literature Search

The Literature Search page allows import of studies to a nest and shows where studies were sourced. This review includes two searches - an API-based (automatic integration) search of PubMed and a file-based import from Embase. Hover and click the "History and Details" column to see greater detail

about the searches, including when they were run and any query structuring available. The PubMed search is API-based and may be run on demand. Hover the Pubmed row and click the “Run” button to update this search- you may import some new records!

INESTED

KNOWLEDGE

Literature Search: Osteoarthritis: Tanezumab

2/2

Nest Home

Dashboard

Literature Search

2/2

Other Sources

Duplicate Review

Search Exploration

Query Builder

Screening

10/10

Configure Exclusion Reasons

Study Inspector

Tagging

36/17

Configure Study Tags

Study Inspector

Extraction

36/17

Study Inspector

Synthesis

Manuscript Editor

Export

Settings

Admin

Searches

Term

Search Engine

Schedule

Search Now

History and Details

Delete

tanezumab AND (osteoarthritis OR arthritis OR OA) AND pain

Other

Never

Last Run: 2023-05-17

Method: file

Results: 96

tanezumab AND (osteoarthritis OR arthritis OR OA) AND ("randomized" ...

PubMed

Never

Run

File

Full History

Other Sources

Records may be imported through other means. Click the “Other Sources” menu item under “Literature Search” to view records that were individually added as expert recommendations. 19 such studies were imported into this Nest. Try importing the DOI or PMID of your favorite study using the “Add by Identifier” form on the right of the page.

INESTED

KNOWLEDGE

Other Sources: Osteoarthritis: Tanezumab

2/2

Nest Home

Dashboard

Literature Search

2/2

Other Sources

Duplicate Review

Search Exploration

Query Builder

Screening

10/10

Configure Exclusion Reasons

Study Inspector

Tagging

36/17

Configure Study Tags

Study Inspector

Extraction

36/17

Study Inspector

Synthesis

Manuscript Editor

Export

Settings

Admin

Add Individual Reference

Bibliomine

Title

Author

Source

Date Added

Added By

Based on minimal clinically important difference values, a mediant...

Di Zhao

Therapeutic Advances in Muscul...

10/8/2022

Jade Thumikam

Efficacy and safety of tanezumab monotherapy or combined with...

Thomas J Scheitler

Ann Rheum Dis

8/13/2021

Nicole Hardy

Efficacy and safety of tanezumab monotherapy or combined with...

Thomas J Scheitler

Ann Rheum Dis

8/13/2021

Nicole Hardy

Safety and efficacy of subcutaneous tanezumab in patients with k...

Charles Bittosa

J Pain Res

8/13/2021

Nicole Hardy

Safety and efficacy of subcutaneous tanezumab in patients with k...

Charles Bittosa

J Pain Res

8/13/2021

Nicole Hardy

Efficacy and safety of intravenous tanezumab for the symptomatic...

Evan Elman

The Journal of Rheumatology

8/10/2021

Nicole Hardy

Efficacy and safety of intravenous tanezumab for the symptomatic...

Evan F Elman

J Rheumatol

8/10/2021

Nicole Hardy

Tanezumab reduces osteoarthritic knee pain: results of a randomi...

Mark Brown

J Pain

6/15/2021

Bernadette Kane

Nerve Growth Factor and Pain Mechanisms

Franziska Denik

Annu Rev Neurosci

6/15/2021

Bernadette Kane

Anti-nerve growth factor in pain management: current evidence

David Chung

J Pain Res

6/15/2021

Bernadette Kane

Efficacy and Safety of Tanezumab on Osteoarthritis Knee and Hip ...

Jurgen Chen

Pain Medicine

6/15/2021

Bernadette Kane

A systematic review of the efficacy and general safety of antiothe...

T J Schmitzer

Osteoarthritis and Cartilage

6/15/2021

Bernadette Kane

Current status of nerve growth factor antibodies for the treatment...

Rachel E Miller

Clin Exp Rheumatol

6/12/2021

Asad Rahmatullah

Nerve growth factor antibody for the treatment of osteoarthritis p...

Martin Schmelz

Pain

6/12/2021

Asad Rahmatullah

Targeting nerve growth factor, a new option for treatment of oste...

Ziqin Cao

Aging (Albany NY)

6/7/2021

Asad Rahmatullah

Pooled analysis of tanezumab efficacy and safety with subgroup a...

Leslie Tive

J Pain Res

6/7/2021

Asad Rahmatullah

Efficacy and safety of tanezumab administered as a fixed dosing re...

Zheng-Rui Fan

Clin Rheumatol

6/4/2021

Asad Rahmatullah

Efficacy and Safety of Tanezumab on Osteoarthritis Knee and Hip ...

Jurgen Chen

Pain Med

6/4/2021

Asad Rahmatullah

Tanezumab for Patients with Osteoarthritis of the Knee: A Meta-A...

Shun-Li Kien

PLoS One

6/4/2021

Asad Rahmatullah

Add by Identifier

Add by Article ID

PubMed ID

DOI

Enter a single or comma separated list of identifiers. Bibliographic data will be automatically imported from PubMed or Crossref

Add Manually

Title

Author Format

First / Last / Full

First Name

Last Name

Publication Date

mm / dd / yyyy

Journal/Source

Publisher

Volume

Issue

Page

Corporate Author

Organization

Link

(URL)

DOI

10-0000/0000

Abstract / Summary

Placeholder

Add Reference

## Screening

Once studies are imported into a nest, they are “Screened” for relevance to the review in the Screening Module. Click the Screening menu header to visit this module.



This screening module displays studies that have yet to be screened, allowing you to decide to include or exclude from the rest of your review and analysis. So far in our review, 110 studies have been screened and 17 included. Try including the last remaining reference by clicking the include button. You may exclude references by selecting an exclusion reason from the drop-down menu and then clicking the exclude button. You may also skip studies you aren't yet sure about, or jump to a prior study, using the buttons under the Navigation menu.

## Abstract Highlighting

Why are study abstracts so colorful? We perform ML-based PICO annotation of abstracts using a model derived from [RobotReviewer](#). To turn off PICO highlighting, toggle off the slide button in the legend just beneath the abstract text.

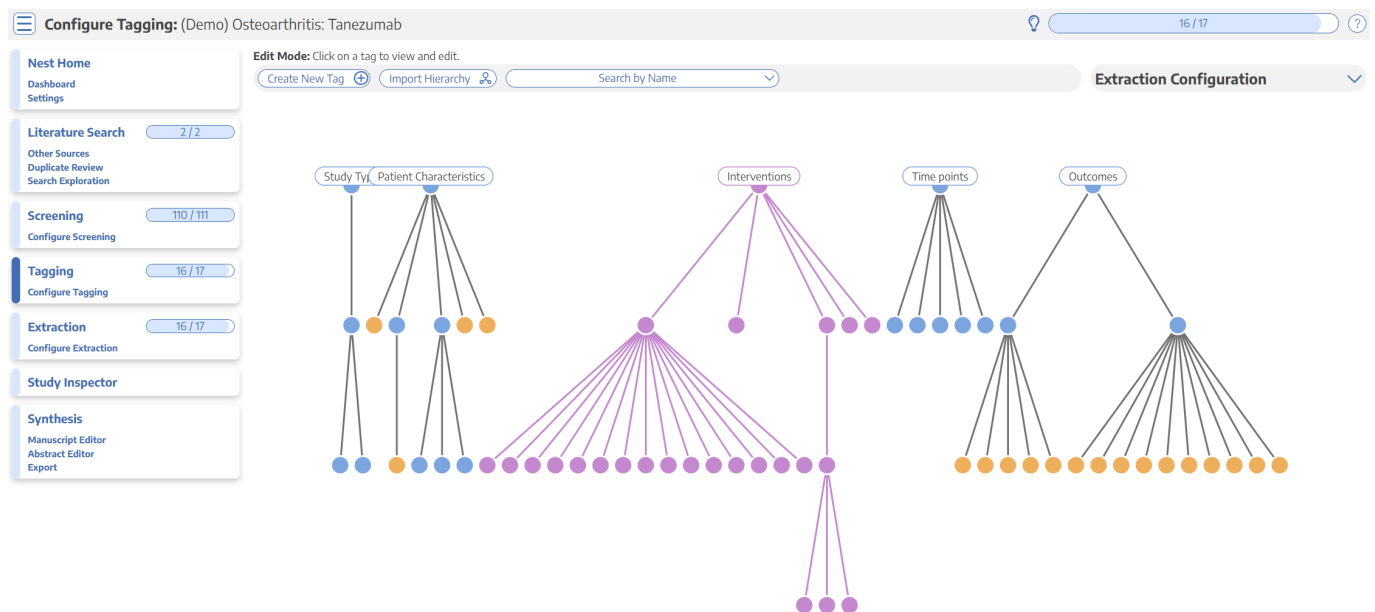
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

## Tagging

The Tagging module allows included studies to be categorized according to their characteristics, such as design, population, outcomes, etc. Nested Knowledge uses hierarchical tags to describe characteristics.

## Tag Hierarchy

Click the “Configure Study Tags” menu item to get started. Tag hierarchies consist of tags (visualized as points) and relationships between them (visualized as connecting lines). The tag hierarchy in this review includes 5 “root” tags - the highest level categories we're considering in the review. Hierarchies should be created and read as a series of “is a” relationships. For example, “Safety Event” is a “Outcome”, “Abnormal Peripheral Sensations” is a “Adverse Event”. Hover around the hierarchy to explore tags and read off the “is a” relationships as you go.



## Tagging Module

Inside the Tagging module, tags may be applied to studies, indicating that a concept is relevant to a study.

**Tagging: Osteoarthritis: Tanezumab**

**Tanezumab reduces osteoarthritic hip pain: results of a randomized, double-blind, placebo-controlled phase III trial.**

**Abstract Full Text Supplements Published**

**Navigation**

**Tagging**

| Tag                                       | Text                       |
|---|----------------------------|
| Rapidly Progressive Osteoarthritis (RPOA) | Upon review of all tota... |
| 10 mg (IV)                                | Patients were randomi...   |
| Female                                    | table 1                    |
| LS means PGA-DA                           | Figure 2                   |
| LS means WOMAC Physical Function (NRS)    | Figure 2                   |
| LS means WOMAC Pain (NRS)                 | Figure 2                   |
| Abnormal Peripartur Sensations            | table 2                    |

**Comments (1)**

**History**

In the Tagging form, select any tag from the dropdown menu, then click Apply Tag; it should now appear in the Tagging Table.

Click a row in the Tagging table that has a non-empty excerpt column to view past applied tags and their “excerpts”, which user-entered text of text, typically extracted from the manuscript, supporting the tag.

## Study Inspector

Study Inspector is the tool in AutoLit for reviewing and searching your past extracted data. Each row in Study Inspector is a study, and columns may be user-selected in the upper left dropdown menu. Studies may be searched into the table by creating Filters. Filters may be created using the Add Filter dropdown menu, but oftentimes the typeahead search bar is fastest. In the below example, we are filtering to studies with a full text uploaded and using the typeahead menu to find all included studies. Try out the title/abstract (TIAB) filter by typing “monotherapy” into the search bar.

Please see our [Extraction Documentation](#) page to review how Extraction was configured for this Nest. Click the Extraction menu item to view and perform Extraction for this review.

The Study Design form specifies intervention arms in the study (placebo and 3 differing Tanezumab dosages, in this case) as well as outcome measurement timepoints in the study (0 and 112 days).



The Extracted Data form contains means, medians, dichotomous rates, and categorical counts corresponding to baseline characteristics and outcomes for the study. Modify some of the data points, which will be auto-saved. If you enter incomplete or invalid data (e.g. a negative value for N), the leading Status column of the table will show a red X. Hover to view the error message.

Synthesis

At this point, we've reviewed all the evidence gathered in AutoLit for the *Osteoarthritis: Tanezumab* Nest. Now let's navigate to Synthesis Home to draw some conclusions from our evidence, by clicking the Synthesis menu heading.

INESTED

KNOWLEDGE

Our Team

Our Vision

Enterprise

AutoLit

Karl

Contributors

Karl Holub

PRISMA

Risk of Bias

Osteoarthritis: Tanezumab

This systematic review and meta-analysis presents 13 randomized controlled trials that analyzed pain and safety outcomes for patients treated with tanezumab for osteoarthritis of the hip or knee. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscale was used at baseline and follow-up and adverse events (AEs), including treatment-related and serious AEs, were reported at follow-up. For 11,388 patients, LS means change-from-baseline for the WOMAC Pain subscale was -9.4 [-10.1, -8.8] across all tanezumab doses, -3.6 [-3.9, -3.2] for placebo, -2.7 [-2.7, -2.6] for naproxen, -2.2 [-2.3, -2.1] for combination therapy, -2.6 [-2.6, -2.6] for oxycodone, -2.4 for non-steroidal anti-inflammatory drugs (NSAIDs), and -1.7 [-1.7, -1.6] for placebo+NSAID. For safety outcomes, AEs were observed among all treatments including 63.3% for oxycodone, 60.3% for NSAIDs, 59.0% for combination therapy, 57.8% for tanezumab, 52.0% for placebo, 50.5% for naproxen, and 34.9% for placebo+NSAID across 6,900 patients. For 973 patients, treatment-related AEs were observed in 40.7%, 17.3%, 15.9%, and 13.5% of the oxycodone, tanezumab, NSAID, and placebo treatments, respectively. For 601 patients, serious AEs were observed in all treatments including 9.7% 5.3%, 4.6%, 3.8%, 2.8%, 2.5% and 2.4% in the combination therapy, placebo+NSAID, NSAID,

Qualitative Synthesis

Browse common concepts discussed in studies of interest. You can interact with the tag diagram to find studies that address your research goals.

Quantitative Synthesis

Examine summary data and statistical analysis. You can compare therapies across outcomes of interest or review evidence from the underlying studies.

Meta-Analysis

| Outcomes                       | Interventions |
|--------------------------------|---------------|
| Abnormal Peripheral Sensations | Placebo       |
| Serious Adverse Events         | 5mg           |
| Any Adverse Events             | 10mg [SC]     |
| LS means PGA-OA                | 2.5mg         |

Manuscript

Read the authors' report of key findings and conclusions. You can also view updated methods, figures, and sources for this review.

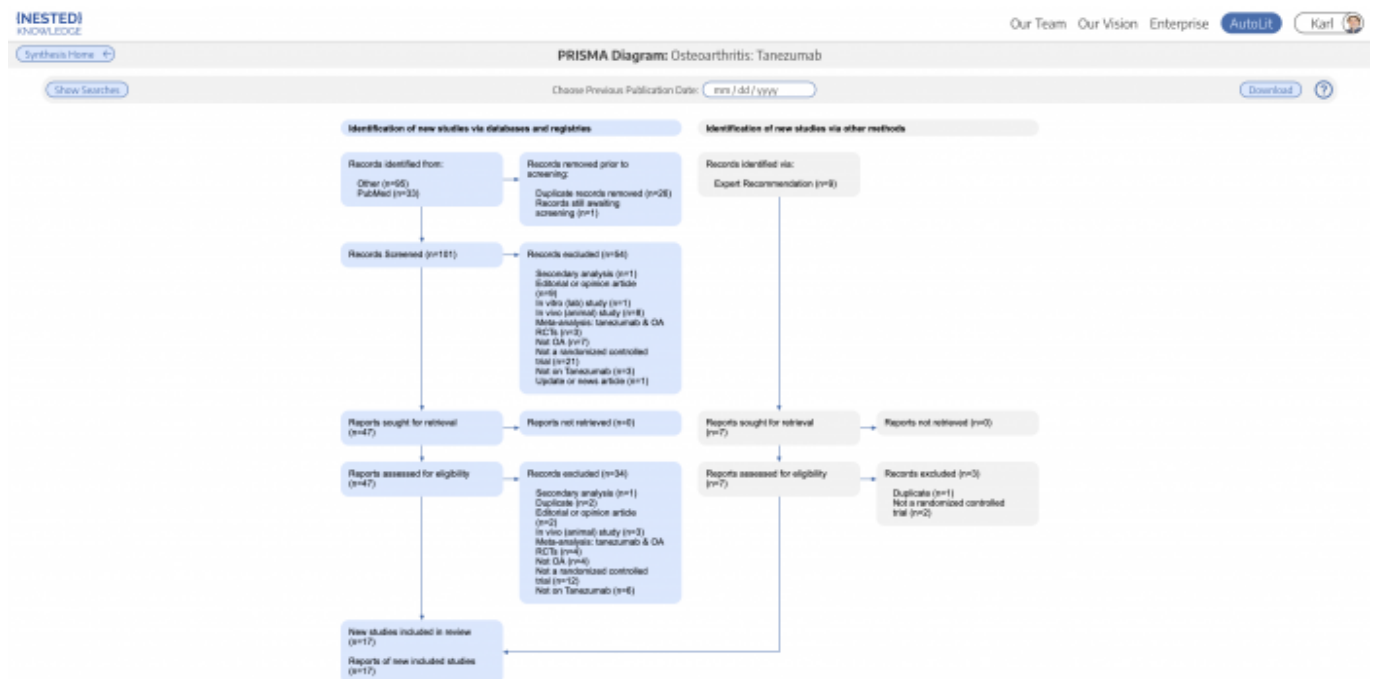
AutoLit

Construct or edit your living systematic review. You can also invite collaborators, share your work, or write a report.

PRISMA

Click the PRISMA button in the bottom left of the page to view a PRISMA 2020 flow diagram. The diagram is auto-populated based on searches imported and studies screened in AutoLit.

Nested Knowledge - <https://wiki.nested-knowledge.com/>

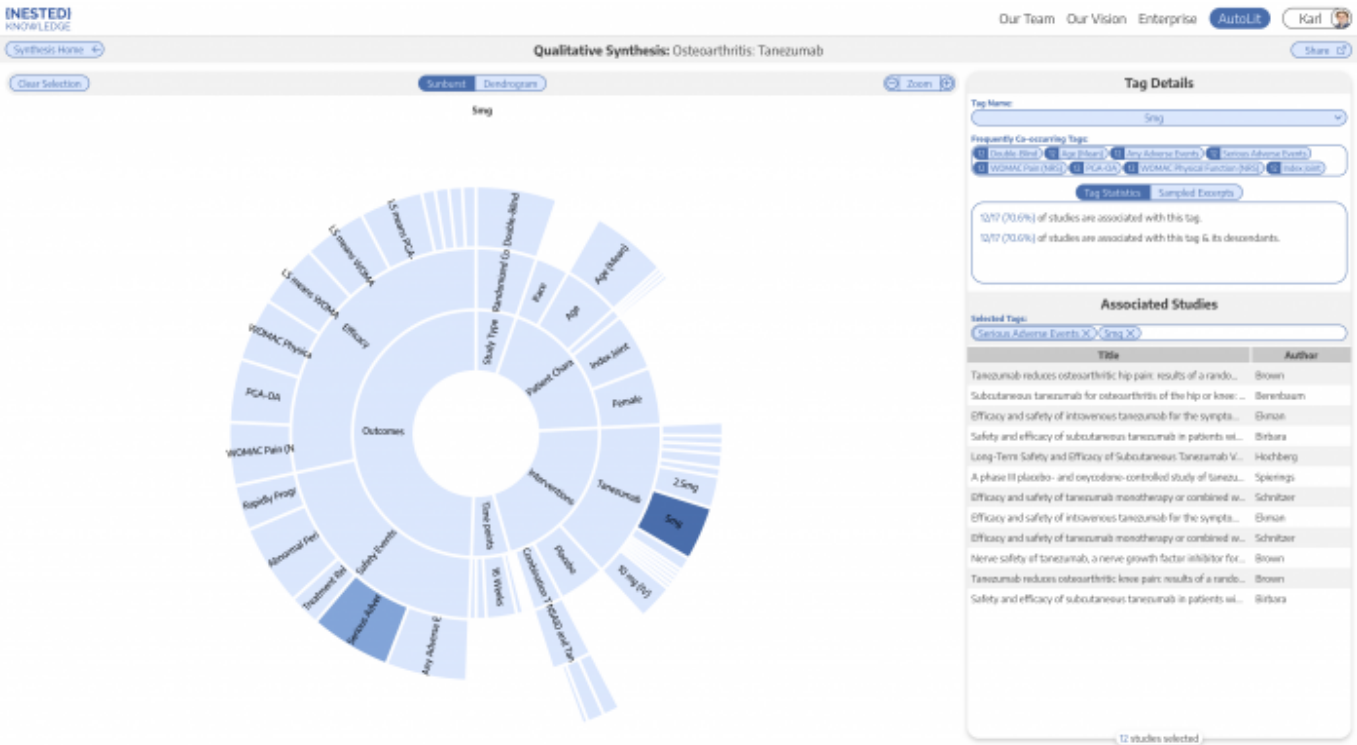


We can see that the 2 searches and 9 (19 - 10 duplicated records already imported in search) expert recommendations are displayed in the diagram. The diagram may be right clicked and saved as an arbitrary resolution SVG or exported in a variety of formats.

## Qualitative Synthesis

Navigate back to Synthesis Home and click the Qualitative Synthesis box. Qualitative Synthesis (QLS) displays data gathered in the Tagging Module. Each slice in the sunburst diagram is a tag. Its width corresponds to how frequently it was applied. Its distance from the center corresponds to its depth in the hierarchy (how many "is a" relationships are between it and its root tag). Click a slice to filter studies displayed to those where the tag was applied. Clicking multiple slices filters to studies with all the selected tags applied. The rightmost bar shows relevant studies (bottom) and some data about the tag (top), like its frequency, excerpts, and tags that were commonly applied with the selected tag.





In this tag selection, we see that some Serious Adverse Event was reported as an outcome in 12 studies that included a 5mg dose as an intervention. Click the rows of the study table to take a deep dive into the extracted data.

Quantitative Synthesis

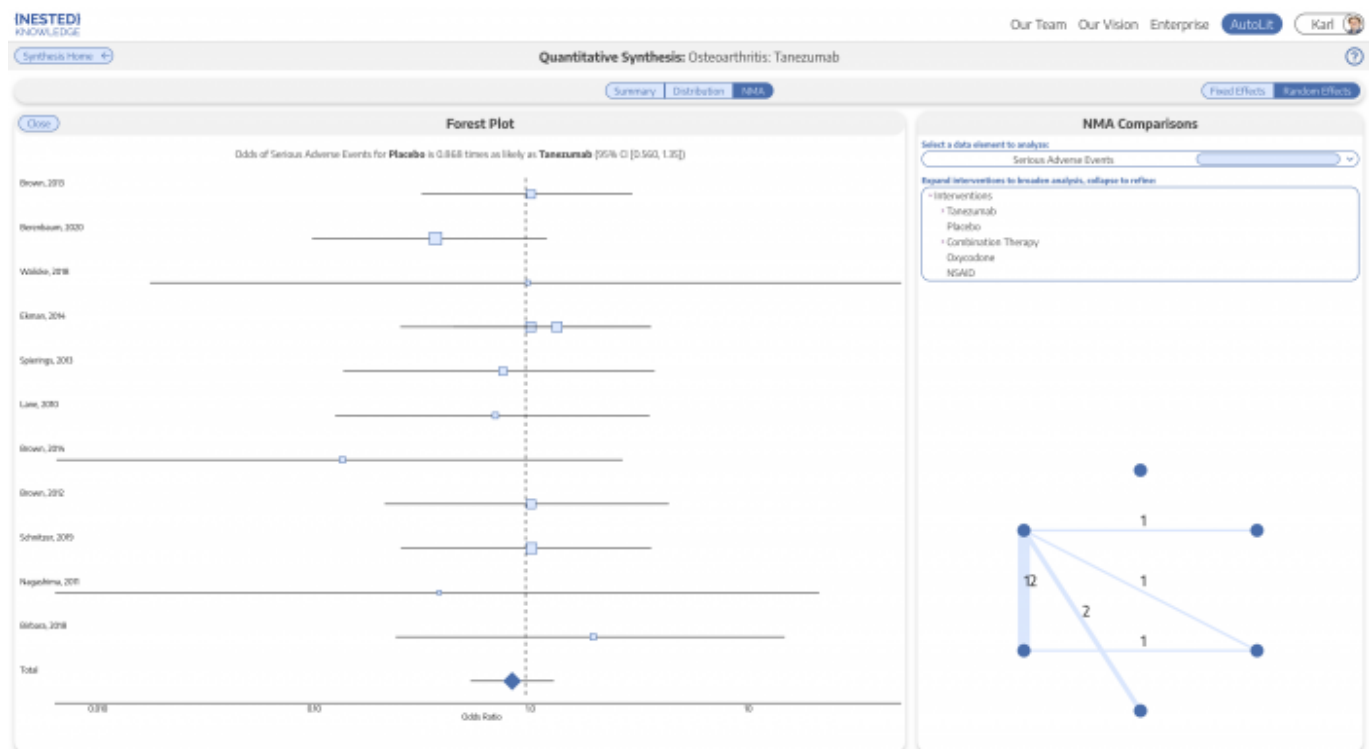
Navigate back to Synthesis Home and click the Quantitative Synthesis box. Quantitative Synthesis (QNS) displays data gathered in the Extraction Module. QNS contains 3 different analyses automatically computed from extracted data.

The Summary tab contains pooled estimates of outcomes, broken out by interventions. Interventions may be expanded to different levels of precision, while outcomes analyzed may be selected from the dropdown menus. In the below example, we find a 49.3% rate of any adverse event for Placebo treatment against 60.7% and 63.4% for Tanezumab and NSAID/Tanezumab combination therapy, respectively

The screenshot displays the INESTED Quantitative Synthesis interface for Osteoarthritis: Tanezumab. The main visualization is a table showing pooled estimates of outcomes, broken out by interventions. The 'Summary' tab is selected, and the 'Any Adverse Events' outcome is chosen.

| Intervention          | Outcome: Abnormal Peripheral Sensations |         |             | Outcome: Serious Adverse Events |       |               | Outcome: Any Adverse Events |       |                |
|-----------------------|---|---------|-------------|---------------------------------|-------|---------------|-----------------------------|-------|----------------|
|                       | Intervention                            | Control | Effect Size | (n/N)                           | %     | [CI]          | (n/N)                       | %     | [CI]           |
| Interventions         | 46                                      | 101     |             | 603/12208                       | 4.3%  | [3.7%, 5.7%]  | 756/12208                   | 59.2% | [56.3%, 62.1%] |
| ↳ Tanezumab           | 101                                     | 101     |             | 376/7865                        | 4.2%  | [3.5%, 5.2%]  | 485/7865                    | 60.7% | [57.3%, 64.1%] |
| ↳ Placebo             | 62                                      | 300     |             | 34/1659                         | 2.4%  | [1.7%, 3.3%]  | 85/1659                     | 49.3% | [44.9%, 53.8%] |
| ↳ Combination Therapy | 2                                       | 2       |             | 14/1530                         | 9.6%  | [7.9%, 11.7%] | 100/1530                    | 63.4% | [53.1%, 72.6%] |
| ↳ NSAID and Tanezumab | 1                                       | 1       |             | 14/1530                         | 9.6%  | [7.9%, 11.7%] | 100/1530                    | 63.4% | [53.1%, 72.6%] |
| ↳ 5 mg + NSAID        | 1                                       | 1       |             | 62/686                          | 9.0%  | [6.6%, 12.2%] | 463/686                     | 65.0% | [50.2%, 78.2%] |
| Balanesou et al.      | 2                                       | 2       |             | 8/150                           | 5.3%  | [2.7%, 10.3%] | 73/150                      | 48.7% | [40.9%, 56.6%] |
| Schritzer et al.      | 1                                       | 1       |             | 25/280                          | 10.0% | [7.0%, 14.7%] | 205/280                     | 73.2% | [67.2%, 78.7%] |
| Schritzer et al.      | 1                                       | 1       |             | 26/256                          | 10.2% | [7.0%, 14.5%] | 185/256                     | 72.3% | [66.5%, 77.4%] |
| ↳ 10 mg + NSAID       | 2                                       | 2       |             | 74/687                          | 10.6% | [7.6%, 14.5%] | 472/687                     | 66.9% | [51.9%, 79.4%] |
| ↳ 2.5 mg + NSAID      | 2                                       | 2       |             | 10/157                          | 7.6%  | [6.4%, 13.0%] | 70/157                      | 45.2% | [37.9%, 53.9%] |
| ↳ Oxycodone           | 1                                       | 1       |             | 4/158                           | 2.5%  | [1.0%, 6.5%]  | 100/158                     | 63.3% | [55.5%, 70.4%] |
| ↳ NSAID               | 1                                       | 1       |             | 46/196                          | 4.8%  | [3.5%, 6.3%]  | 604/196                     | 60.3% | [57.3%, 63.3%] |

The NMA tab computes a Network Meta-Analysis, which estimates effect sizes between pairwise comparisons of interventions on an outcome. The NMA comes with a network diagram (showing how commonly interventions were compared with one another), an effect size matrix, and forest plots (accessed by clicking on a cell in the effects matrix). Use the intervention expansion menu on the right of the page to refine interventions analyzed.



## Closing Remarks

You've now seen how a review may be completed & shared with the Nested Knowledge platform. We encourage you to head back to AutoLit and explore the variety of configuration options, and ever-growing feature set we didn't get to cover here. If you're feeling ambitious, start your own Nest from scratch!

Use this documentation to guide you through more complex topics, and as always, please reach out to our support team via email and make requests on [Nolt](#).

From:  
<https://wiki.nested-knowledge.com/> - **Nested Knowledge**

Permanent link:  
<https://wiki.nested-knowledge.com/doku.php?id=wiki:start:demo:osteoarthritis>

Last update: **2023/06/27 21:52**