

# 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

The screenshot displays the 'Nest Home' interface for 'Osteoarthritis: Tanezumab'. On the left is a navigation menu with options like 'Literature Search', 'Screening', 'Tagging', 'Extraction', 'Synthesis', and 'Settings'. The main content area includes an 'About' section, a 'Review Title' section, and an 'Authors' table. The 'Comments' section on the right shows a discussion between users.

**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 "?" 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. Efforts to manuscript. Senior author/study coordinator	NK
Mohamed Abdelmegeed	Wrote the manuscript. First author/corresponding author	SME
John Pedersen	Performed meta-analysis. Second author	SME/NK
Kevin Kallmes	Provided general guidance on project.	NK
Bernadette Kane	Did 25% of nest.	NK
Azad Rahmarullah	Did 25% of nest and tables	NK
Kathryn Cowie	Did some tables	NK
Kristen Hutchison	Did ROB	NK
Ranika Tardund	Did ROB	NK

**Comments**

Mohamed Abdelmegeed 3/10/23, 12:49 PM

@Kevin Kallmes

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 hGF 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 pain soon. Hsiehberg, 2025 noted that anti-hGF treatment may lead to treatment-related rapidly progressive OA (RPROA) and osteonecrosis (PMID: 3522292), and that Tanezumab combined with NSAIDs treatment appeared to increase the risk of RPROA, relative to Tanezumab monotherapy (PMID: 26554876). A partial clinical hold 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; 31257163)). The maximum dose of Tanezumab was reduced from 10 mg to 5mg after [FDA's partial clinical hold](#).

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!

The screenshot shows the INESTED Literature Search interface. The search query is 'tanezumab AND (osteoarthritis OR arthritis OR OA) AND pain'. The search engine is PubMed, and the search was last run on 2022-05-17. The results show 95 records. The interface includes a sidebar with navigation options like Literature Search, Screening, Tagging, Extraction, Synthesis, and Settings.

## 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.

The screenshot shows the INESTED Other Sources interface. It displays a table of 19 records imported from other sources. The table has columns for Title, Author, Source, Date Added, and Added By. On the right side, there are two forms: 'Add by Identifier' and 'Add Manually'. The 'Add by Identifier' form has fields for PubMed ID, DOI, and a list of identifiers. The 'Add Manually' form has fields for Title, Author, Journal/Source, Volume, Issue, and Link.

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 Bibasa	J Pain Res	8/13/2021	Nicole Hardy
Safety and efficacy of subcutaneous tanezumab in patients with k...	Charles Bibasa	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 Denk	Anne Rev Neurosci	6/15/2021	Bernadette Kane
Anti-nerve growth factor in pain management: current evidence	David Chang	J Pain Res	6/15/2021	Bernadette Kane
Efficacy and Safety of Tanezumab on Osteoarthritis Knee and Hip...	Jurquan Chen	Pain Medicine	6/15/2021	Bernadette Kane
A systematic review of the efficacy and general safety of antibo...	T. J. Schnitzer	Osteoarthritis and Cartilage	6/15/2021	Bernadette Kane
Current status of nerve growth factor antibodies for the treatmen...	Rachel E Miller	Clin Exp Rheumatol	6/12/2021	Azad Rahmatullah
Nerve growth factor antibody for the treatment of osteoarthritis p...	Martin Schmalz	Pain	6/12/2021	Azad Rahmatullah
Targeting nerve growth factor, a new option for treatment of oste...	Ziqin Cao	Aging (Albany NY)	6/7/2021	Azad Rahmatullah
Pooled analysis of tanezumab efficacy and safety with subgroup a...	Leslie Tive	J Pain Res	6/7/2021	Azad Rahmatullah
Efficacy and safety of tanezumab administered as a fixed dosing re...	Zheng-Rui Fan	Clin Rheumatol	6/4/2021	Azad Rahmatullah
Efficacy and Safety of Tanezumab on Osteoarthritis Knee and Hip...	Jurquan Chen	Pain Med	6/4/2021	Azad Rahmatullah
Tanezumab for Patients with Osteoarthritis of the Knee: A Meta-A...	Shun-Li Han	PLoS One	6/4/2021	Azad Rahmatullah

## 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.

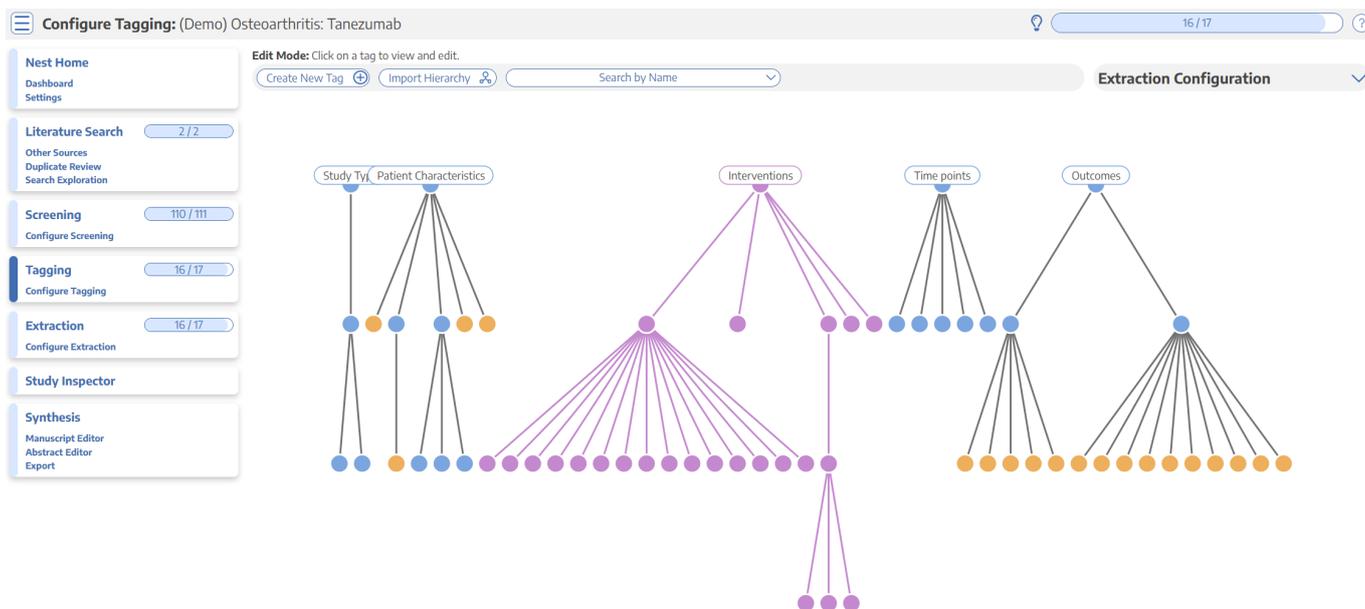
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

## 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 a you go.



## Tagging Module

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

The screenshot displays the INESTED Knowledge interface. On the left, a sidebar contains navigation options: Next Home, Literature Search (with 777 results), Screening (193/111), Tagging (36/10), Extraction (36/10), Synthesis, and Settings. The main area shows a document viewer for the paper "Tanezumab Reduces Osteoarthritic Hip Pain: Results of a Randomized, Double-Blind, Placebo-Controlled Phase III Trial". The document text is visible, including the title, authors (Mark T. Brown, Frederick T. Murphy, David M. Radin, Isabelle Davignon, Michael D. Smith, and Christine R. West), and abstract. On the right, a "Tagging" sidebar is active, showing a table of tags and their associated text excerpts. The table includes tags like "Progressive Osteoarthritis (PROA)", "10 mg (IV)", "Female", "LS means PGA-DA", "LS means WOMAC Physical Function (WPS)", and "LS means WOMAC Pain (PWS)". Below the table, there is a "Select Tag" dropdown, an "Enter Text" input field, and an "Apply Tag" button. At the bottom of the sidebar, there are sections for "Comments (1)" and "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 pieces 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.

**Study Inspector**

Title	Publication Year	Screening Status
Anti-nerve growth factor in pain management: current evidence	2016	Excluded: Not a randomized controlled trial
Long-term open-label study of tanezumab for moderate to severe osteoarthritis pain	2011	Excluded: Not a randomized controlled trial
Efficacy and safety of intra-articular injection of tropicamide in patients with osteoarthritis of the knee	2019	Excluded: Not on Tanezumab
A fully human anti-NGF monoclonal antibody for the treatment of osteoarthritis pain	2013	Excluded: In vivo (animal) study
Imaging atlas for eligibility and on-study safety of potential tanezumab treatment sites in patients with osteoarthritis of the knee	2016	Excluded: Not a randomized controlled trial
Safety, tolerability, pharmacokinetics, and efficacy of AMG 403, a fully human anti-nerve growth factor antibody, in patients with osteoarthritis of the knee	2015	Excluded: Not on Tanezumab
Imaging atlas for eligibility and on-study safety of potential tanezumab treatment sites in patients with osteoarthritis of the knee	2016	Excluded: Not a randomized controlled trial
Tanezumab reduces osteoarthritic hip pain: results of a randomized, double-blind, placebo-controlled phase III trial	2013	Included
Human osteocyte expression of Nerve Growth Factor: The effect of mechanical loading	2019	Excluded: Not a randomized controlled trial
Subcutaneous tanezumab for osteoarthritis of the hip or knee: a randomized, double-blind, placebo-controlled phase III trial	2020	Included
TGF-beta is a potent inducer of Nerve Growth Factor in articular chondrocytes	2016	Excluded: Editorial or opinion article
Tanezumab reduces osteoarthritic knee pain: results of a randomized, double-blind, placebo-controlled phase III trial	2012	Excluded: Duplicate
Responsiveness of Single versus Composite Measures of Pain in Osteoarthritis	2018	Excluded: Not a randomized controlled trial
Efficacy and safety of tanezumab added on to diclofenac sodium in patients with osteoarthritis of the knee	2014	Included
First-in-human randomized clinical trials of the safety and efficacy of tanezumab in patients with osteoarthritis of the knee	2011	Included
Onset and maintenance of efficacy of subcutaneous tanezumab in patients with osteoarthritis of the knee	2020	Excluded: Secondary analysis
Fibronectin in patients with interstitial cystitis/bladder pain syndrome	2017	Excluded: Not OA
Efficacy and safety of tanezumab in patients with chronic low back pain	2021	Excluded: Not OA
A systematic review of the efficacy and general safety of anti-nerve growth factor antibodies in patients with osteoarthritis	2016	Excluded: Not a randomized controlled trial
Efficacy and safety of intravenous tanezumab for the symptomatic treatment of osteoarthritis of the knee	2014	Included
Serious joint-related adverse events in randomized controlled trials of tanezumab in patients with osteoarthritis	2016	Excluded: Not a randomized controlled trial
Nerve growth factor inhibition with tanezumab influences weight loss in patients with osteoarthritis of the knee	2017	Excluded: In vivo (animal) study
Model-based evaluation of cost-effectiveness of nerve growth factor inhibition with tanezumab in patients with osteoarthritis of the knee	2016	Excluded: Not a randomized controlled trial
Effectiveness of tanezumab as a novel treatment for the management of osteoarthritis of the knee	2018	Excluded: Not OA

## Extraction

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.

**Data Extraction: Osteoarthritis: Tanezumab**

**Tanezumab Reduces Osteoarthritic Hip Pain: Results of a Randomized, Double-Blind, Placebo-Controlled Phase III Trial**

Mark T. Brown,<sup>1</sup> Frederick T. Murphy,<sup>2</sup> David M. Radin,<sup>3</sup> Isabelle Davignon,<sup>4</sup> Michael D. Smith,<sup>5</sup> and Christine R. West<sup>1</sup>

**Abstract**

**Objective:** To compare the efficacy of tanezumab versus placebo for reducing pain and improving physical function in patients with osteoarthritis (OA) of the hip.

**Methods:** This was a 32-week, randomized, double-blind, placebo-controlled, phase III trial. Patients with baseline Western Ontario and MacMaster Universities (OASIS) Pain and Physical Function subscale scores of 55 and 24, respectively, and patient's global assessment of OA as "fair," "poor," or "very poor" were treated at baseline and weeks 8 and 16. Coprimary efficacy end points were change from baseline to week 16 in WOMAC Pain and Physical Function subscale and patient's global assessment, analyzed using analysis of covariance. Adverse events (AEs) were monitored throughout.

**Results:** Patients (n = 621) were randomized 1:1:1:1 to treatment with intravenous tanezumab 2.5 mg, 5 mg, or 10 mg or placebo. Each tanezumab group showed significant improvement for the 3 coprimary end points versus placebo (P < 0.001 for all). AE incidence ranged from 8% to 88% across tanezumab groups versus 40% for placebo. Safety findings were similar to those previously reported. The tanezumab OA clinical program was temporarily placed on hold because of AEs leading to joint replacement. Total joint replacements were reported in 8 patients (1 in the 10 mg, 2 in the 5 mg, 2 in the 2.5 mg, and 3 in the placebo group; a total of 9 joints were replaced (8 hips [7 index joints] and 1 shoulder).

**Conclusion:** Our findings indicate that tanezumab provides superior pain relief and improvement in physical function and patient's global assessment versus placebo in patients with painful hip OA, and is generally well tolerated.

Approximately 12% of adults in the US develop osteoarthritis (OA) (1), with moderate-to-severe disease occurring in 2-10% of whites and <1% of their Indian, African Americans, Hong Kong Chinese, and Native Americans (2). Current treatment options for painful OA of the hip are largely inadequate. Nonsteroidal antiinflammatory drugs and opioid analgesics are commonly used (3). However, these medications have proven gastrointestinal and cardiovascular side effects (4,5) and, for some patients, result in an unsatisfactory therapeutic response. Potent analgesic medications that are well tolerated may help to avoid or delay surgical intervention (6).

Nerve growth factor (NGF) is a neurotrophin that regulates the structure and function of NGF-responsive sensory neurons, including small-diameter nociceptive afferent neurons (nerve fiber development)

**Navigation**

**Study Design**

Status	Intervention	Arm Size
✓	10mg SC	150
✓	5mg	154
✓	2.5mg	155
✓	Placebo	155

**Measurement Points**

Status	Timepoint	Value	Units
✓	Baseline	0	days
✓	Outcome	112	days

**Extracted Data**

**Abnormal Peripheral Sensations**

Status	Arm	Peripheral neuropathy	Hypoesthesia	Paraesthesia
✓	10mg SC	3	3	3
✓	5mg	0	2	4
✓	2.5mg	2	4	3
✓	Placebo	0	3	5

**Age (Mean)**

Status	Arm	Mean	Range Lower	Range Upper	N
✓	10mg SC	65.5	35	102	157
✓	5mg	63.8	25	86	154
✓	2.5mg	62.4	26	86	155
✓	Placebo	62.9	28	86	155

**Any Adverse Events**

Status	Arm	Events	Total
✓	10mg SC	89	157
✓	5mg	84	154
✓	2.5mg	90	155
✓	Placebo	60	155

**Female**

Status	Arm	Events	Total
✓	10mg SC	86	157
✓	5mg	92	154
✓	2.5mg	101	155

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.

**Contributors**  
Karl Hakub

**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 2.6% in the combination therapy, placebo+NSAID, NSAID,

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

**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.

Tag	Frequency
Double Blind	18
Abnormal Peripheral Sensations	18
Serious Adverse Events	18
Any Adverse Events	18

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

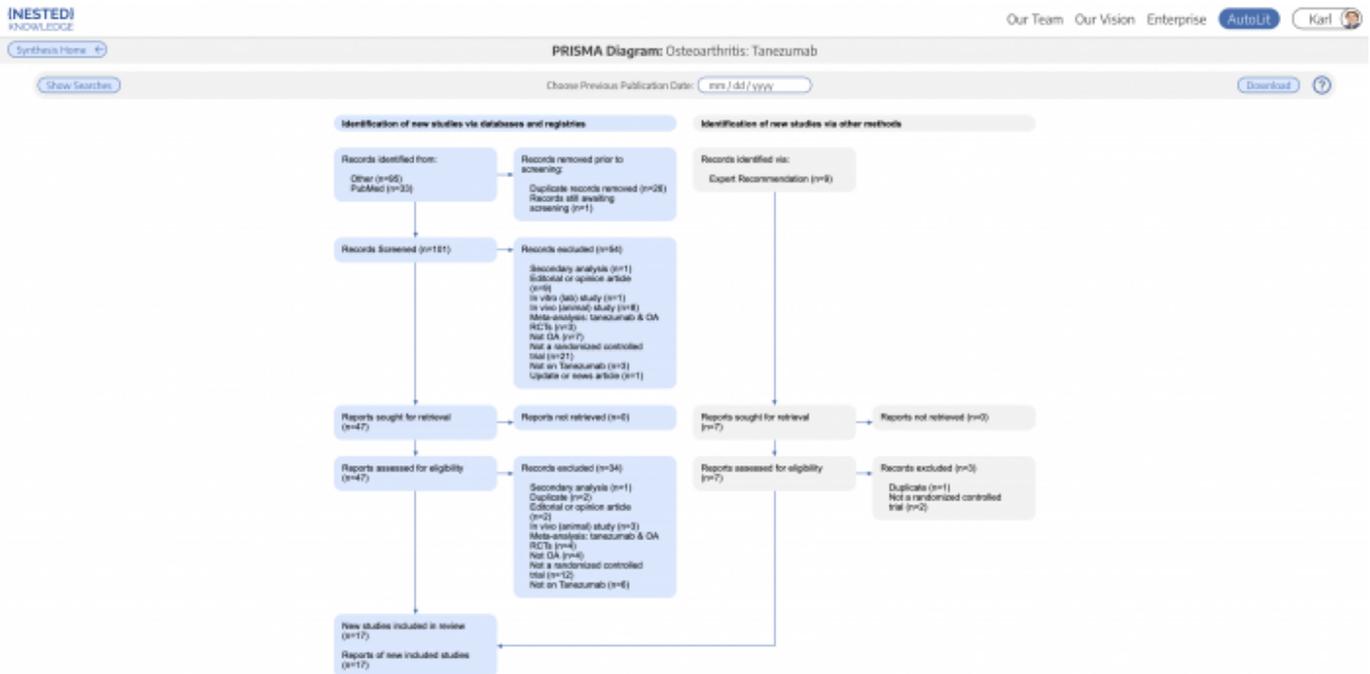
Outcomes	Interventions
Abnormal Peripheral Sensations	Placebo
Serious Adverse Events	5mg
Any Adverse Events	10mg [SC]
LS means PGA-DA	2.5mg

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

PRISMA  
Risk of Bias

## 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.



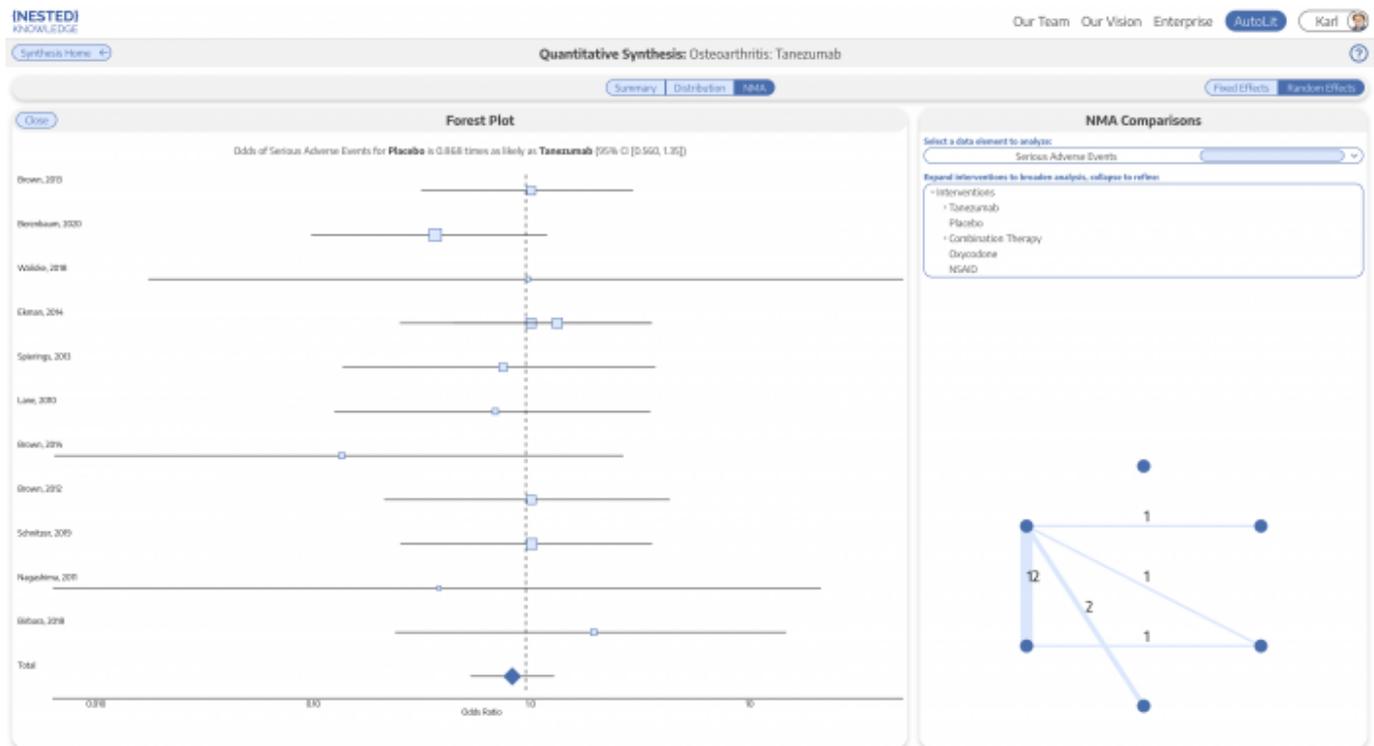
We can see that the 2 searches and 9 (19 - 10 duplicated records already imported in search) expert recommendations are displayed in the diagram. The diagram may be right clicked and saved as an arbitrary resolution SVG or exported in a variety of formats.

## 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.



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](#).

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