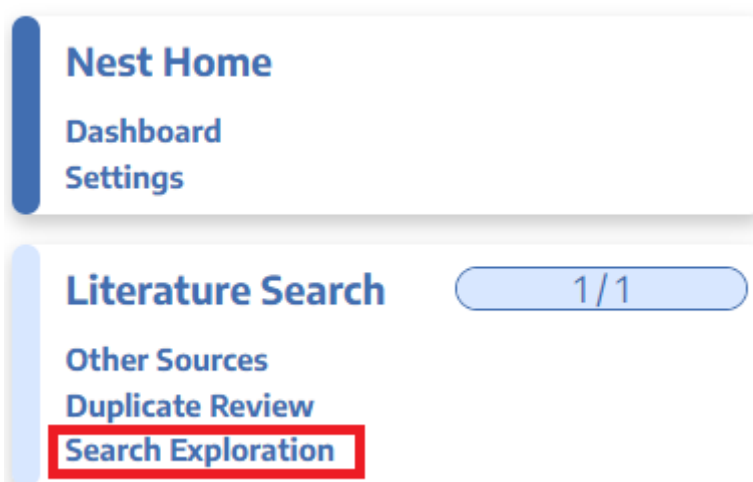


Search Exploration

The Search Exploration page allows you to generate search terms based on central concepts of your nest. Enter your Population, Interventions (and Comparators), and Outcomes (PICO) to generate a Boolean query that can be used on PubMed, and explore potential search results' abstracts, key terminology, and topics of interest to help construct your final search strategy. When complete, proceed to [Lit Search](#) and [Run your Search](#).

How to Begin Search Exploring

1. Navigate to Search Exploration

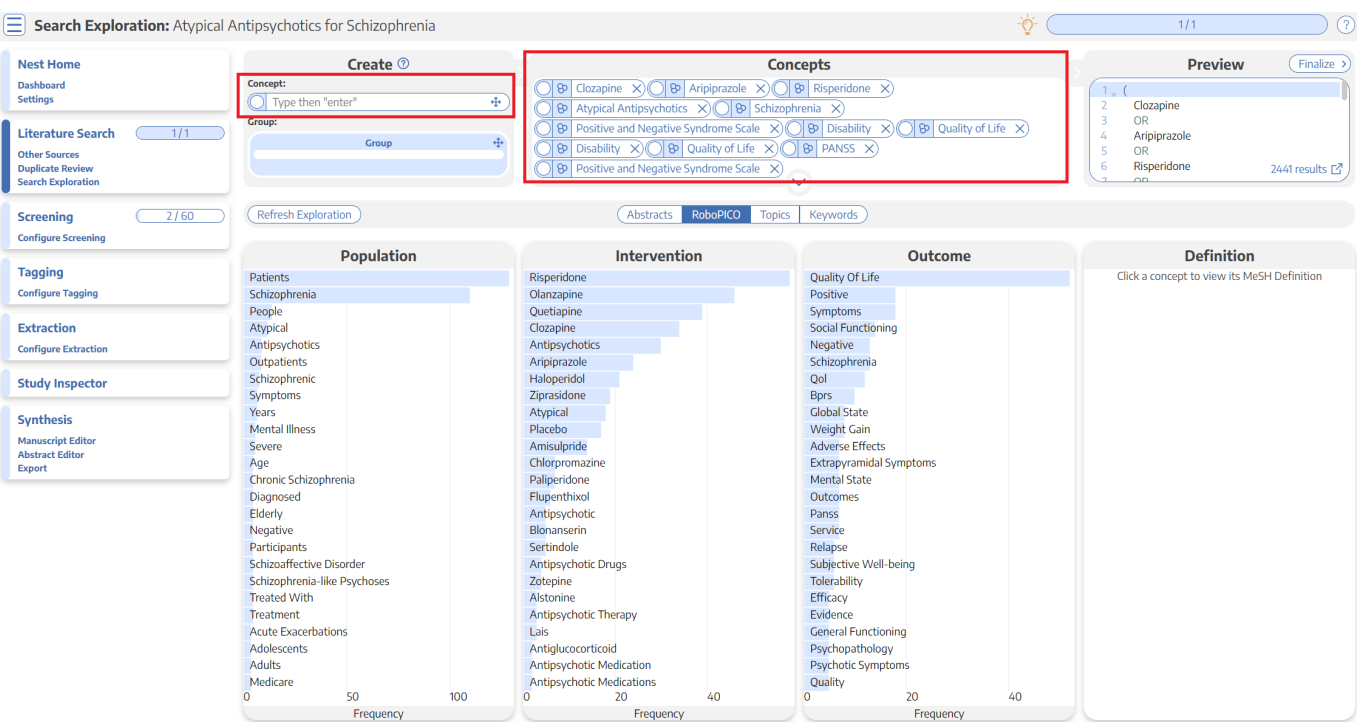


2. Enter PICO of Interest:

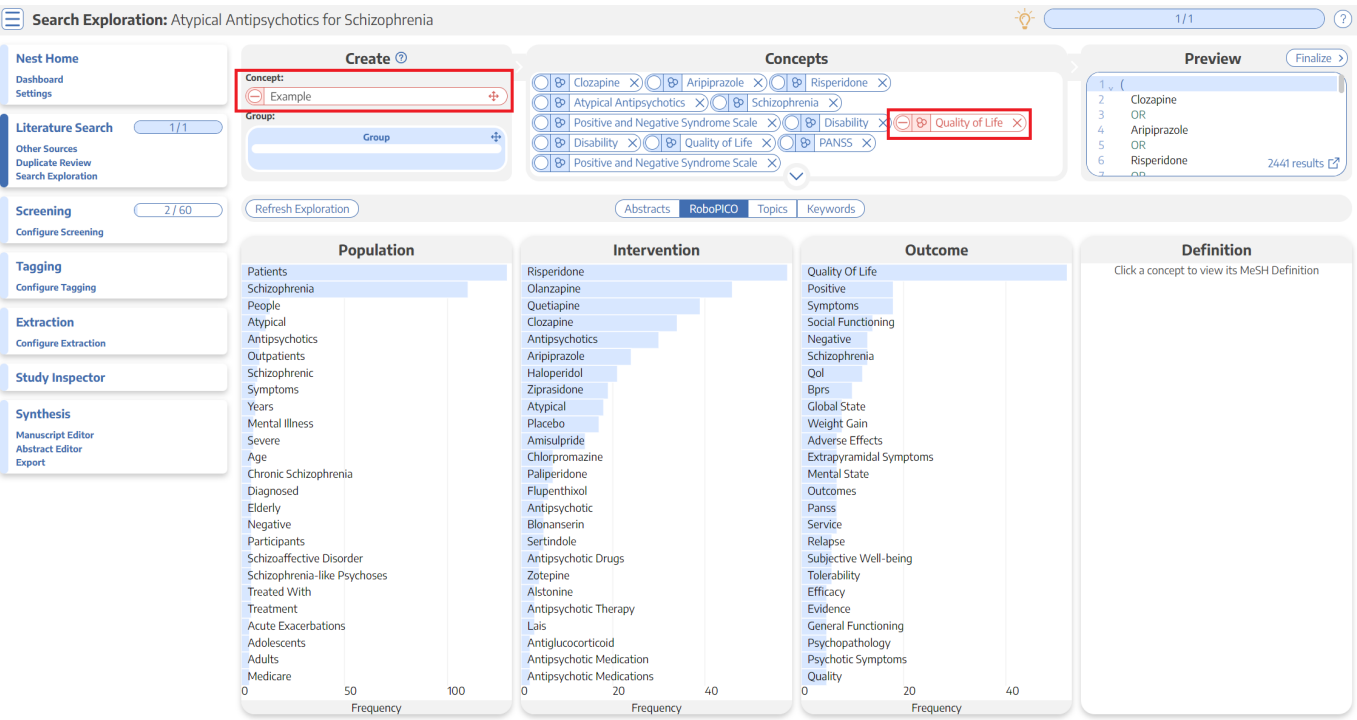
When you create a nest, you will have the option to add details about the Population, Interventions (and comparators), and Outcomes (PICO).

Imagine you are asking the Research Question: How do atypical antipsychotics (I) impact the quality of life and disability (O) in adults with schizophrenia (P)?

1. First, enter the Population (patients with schizophrenia), Interventions (atypical antipsychotics), and Outcomes (disability and quality of life) in the Concept bar under Create.
2. Enter each concept, then hit the Enter button, this will move them under Concepts.
3. Continue adding terms until you have enough terms to identify your specific topic area (**Recommended:** 2 to 5 terms per category).



What is a **Comparator**? A comparator is the drug, device, or intervention that the main intervention is tested against. Typical comparator arms include placebo and standard of care (SOC). In the framework shown here, comparators can be included under interventions.



Negation: Check the negate box to exclude the specific PICO elements from your search. For example, you can add the population “Pediatric” and negate it if you would like to



exclude pediatric populations from your research question.

3. Edit Concepts

When you have completed the tasks above, you will have unstructured concepts of interest, but no grouping of terms and no information yet populated to the Abstracts, RoboPICO, Topic Modeling, and Keywords.

To proceed, click on the down arrow under Concepts to view, add, and group together PICO elements. Alternatively, you can drag and drop a group into the concepts box to expand.

4. Group together PICO elements

1. Drag and drop the Group box into the concepts box.
2. Group together sets of populations, interventions, or outcomes. This group will function like the OR operator in search strings. In this example, specific types of antipsychotic medications are grouped together.
3. You can also negate whole groups by checking the box next to Negate.

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Create

Concept:
Type then "enter"

Group:
Group

Concepts

Intervention
Clozapine X Aripiprazole X Risperidone X Atypical Antipsychotics X
Negate
Population
Schizophrenia X
Negate
Outcome
Positive and Negative Syndrome Scale X Disability X Quality of Life X
Disability X Quality of Life X PANSS X
Positive and Negative Syndrome Scale X
Negate
Drag & Drop
Negate

Preview

Finalize

1 (Clozapine
2 OR
3 Aripiprazole
4 OR
5 Risperidone
6 OR
7 Atypical Antipsychotics
8)
9 AND
10 (Schizophrenia
11)
12 AND
13 (Positive and Negative Syndrome Scale
14 OR
15 Disability
16 OR
17 Quality of Life
18 OR
19 Disability
20 OR
21 Quality of Life
22 OR
23 PANSS
24 OR
25 Positive and Negative Syndrome Scale
26)
27)
28)
29)

2441 results

Refresh Exploration

Abstracts

RoboPICO

Topics

Keywords

5. Run or Update Search Exploration

To populate Abstracts, RoboPICO, Topic Modeling, and Keywords:

- Select the “Refresh Exploration” button

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Create

Concept:
Example

Group:
Group

Concepts

Clozapine X Aripiprazole X Risperidone X
Atypical Antipsychotics X Schizophrenia X
Positive and Negative Syndrome Scale X Disability X Quality of Life X
Disability X Quality of Life X PANSS X
Positive and Negative Syndrome Scale X

Preview

Finalize

1 (Clozapine
2 OR
3 Aripiprazole
4 OR
5 Risperidone
6)
7)

2441 results

Refresh Exploration

Abstracts

RoboPICO

Topics

Keywords

Population

Patients
Schizophrenia
People
Atypical
Antipsychotics
Outpatients
Schizophrenic
Symptoms
Years
Mental Illness
Severe
Age
Chronic Schizophrenia
Diagnosed
Elderly
Negative
Participants
Schizoaffective Disorder
Schizophrenia-like Psychoses
Treated With
Treatment
Acute Exacerbations
Adolescents
Adults
Medicare

Frequency

Intervention

Risperidone
Olanzapine
Quetiapine
Clozapine
Antipsychotics
Aripiprazole
Haloperidol
Ziprasidone
Atypical
Placebo
Amisulpride
Chlorpromazine
Paliperidone
Flupenthixol
Antipsychotic
Blonanserin
Sertindole
Antipsychotic Drugs
Zotepine
Alstonine
Antipsychotic Therapy
Lais
Antiglucocorticoid
Antipsychotic Medication
Antipsychotic Medications

Frequency

Outcome

Quality Of Life
Positive
Symptoms
Social Functioning
Negative
Schizophrenia
Qol
Bprs
Global State
Weight Gain
Adverse Effects
Extrapyramidal Symptoms
Mental State
Outcomes
Panss
Service
Relapse
Subjective Well-being
Tolerability
Efficacy
Evidence
General Functioning
Psychopathology
Psychotic Symptoms
Quality

Frequency

Definition

Click a concept to view its MeSH Definition

- A modal will appear while Search Exploration refreshes. This may take a minute, since this will run a pre-search of PubMed.

Refreshing Exploration Records

We're retrieving a sample of up to 100 new records that better match your newly added concepts. Please wait while we retrieve records from PubMed and run our language models against them. Once this import is complete, the records and visuals you are exploring will be automatically updated.

Search Exploration Record Update

Ingested 100 studies into your Nest. Processing new studies...

Close

When you update search exploration, the references in your nest **will not change**. The records and data returned from this step will only be used for Search Exploration.

How to Interpret Search Exploration Findings

There are several ways to explore the references pulled by your exploratory search. The goal of this process should be to **expand or refine your search terms** so that they return as many records of interest while limiting irrelevant results.

Iterative Refinement: As you use the tools outlined below to add, remove, or restructure your terms, you should periodically re-run "Update Search Exploration", as this is **only run manually**, and not automatically updated.

1. Abstracts

Skim through abstracts retrieved through your search exploration terms.

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Create

Concept: Mortality

Group:

Refresh Exploration

Concepts

Clozapine

Atypical Antipsychotics

Positive and Negative Syndrome Scale

Disability

Quality of Life

PANSS

Positive and Negative Syndrome Scale

Aripiprazole

Schizophrenia

Risperidone

Disability

Quality of Life

PANSS

Abstracts

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Topics

Keywords

Preview

Finalize

1

2

3

4

5

6

7

Clozapine

OR

Aripiprazole

OR

Risperidone

1630 results

Navigation

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References

Title	Year
Polygenetic risk scores and phenotypic constellations of obsessive-compulsive disorder in clozapine-treated schizophrenia.	2023
Striatum-related spontaneous coactivation patterns predict treatment response on positive symptoms of drug-naïve first-episode schizophrenia with risperidone monotherapy.	2023
Establishment of an assistive diagnostic model for schizophrenia with oxidative stress biomarkers.	2023
Verbal and visual learning ability in patients with treatment-resistant schizophrenia: A 1-year follow-up study.	2023
Effects of zinc sulfate on schizophrenia symptoms in patients undergoing atypical antipsychotic pharmacotherapy.	2022
A case study of the utilization of clozapine treatment for treatment-resistant schizophrenia associated with 22q11.2 deletion syndrome.	2023

Polygenetic risk scores and phenotypic constellations of obsessive-compulsive disorder in clozapine-treated schizophrenia.

Obsessive-compulsive symptoms (OCS) are frequently observed in individuals with schizophrenia (SCZ) treated with clozapine (CLZ). This study aimed to analyze prevalence of OCS and obsessive-compulsive disorder (OCD) in this subgroup and find possible correlations with different phenotypes. Additionally, this is the first study to examine polygenetic risk scores (PRS) in individuals with SCZ and OCS. A multicenter cohort of 91 individuals with SCZ who were treated with CLZ was recruited and clinically and genetically assessed. Symptom severity was examined using the Positive and Negative Symptom Scale (PANSS), Clinical Global Impression Scale (CGI), the Calgary Depression Scale for Schizophrenia (CDSS), Global Assessment of Functioning Scale (GAF) and Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). Participants were divided into subgroups based on phenotypic OCS or OCD using Y-BOCS scores. Genomic-wide data were generated, and PRS analyses were performed to evaluate the association between either phenotypic OCD or OCS severity and genotype-predicted predisposition for OCD, SCZ, cross-disorder, and CLZ/norclozapine (NorCLZ) ratio, CLZ metabolism and NorCLZ metabolism. OCS and OCD were frequent comorbidities in our sample of CLZ-treated SCZ individuals, with a prevalence of 39.6% and 27.5%, respectively. Furthermore, the Y-BOCS total score correlated positively with the duration of CLZ treatment in years ($r = 0.28$; $p = 0.008$) and the PANSS general psychopathology subscale score ($r = 0.23$; $p = 0.028$). A significant correlation was found between OCD occurrence and PRS for CLZ metabolism. We found no correlation between OCS severity and PRS for CLZ metabolism. We found no correlation for either OCD or OCS and PRS for OCD, cross-disorder, SCZ, CLZ/NorCLZ ratio or NorCLZ metabolism. Our study was able to replicate previous findings on clinical characteristics of CLZ-treated SCZ individuals. OCS is a frequent comorbidity in this cohort and is correlated with CLZ treatment duration in years and PANSS general psychopathology subscale score. We found a correlation between OCD and PRS for CLZ metabolism, which should be interpreted as incidental for now. Future research is necessary to replicate significant findings and to assess possible genetic predisposition of CLZ-treated individuals with SCZ to OCS/OCD. Limitations attributed to the small sample size or the inclusion of subjects on co-medication must be considered. If the association between OCD and PRS for CLZ metabolism can be replicated, it should be further evaluated if CYP1A2 alteration, respectively lower CLZ plasma level, is relevant for OCD development.

Population/Problem

Intervention

Outcome

Your Keywords

The purpose of reviewing Abstracts should be to:

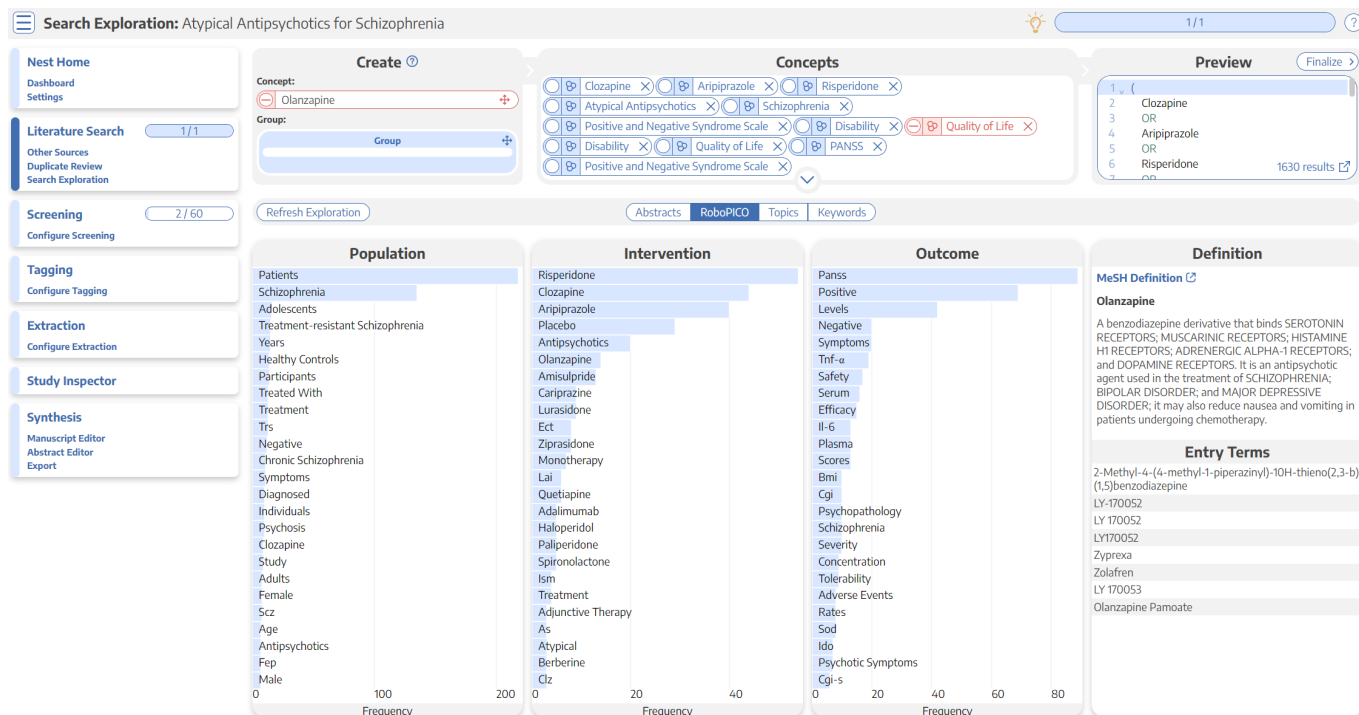
1. Confirm that your search is returning relevant records, and
2. Identify the key terms found in relevant records and adding them to your PICO terms.

2. RoboPICO

Browse commonly-mentioned Populations, Interventions, and Outcomes from abstracts and titles. PICO elements are identified by RoboPICO, which is an open source fork of the models offered in RobotReviewer.

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The purpose of RoboPICO should be to:

1. Identify the most common topics of underlying abstracts, and
2. Identify terms that you should add to your PICO (which you can populate to "Add a PICO Element" by clicking on the relevant row).

Clicking a row in the chart also initiates a strict MeSH lookup on the PICO element; not all extracted PICO elements will correspond to MeSHs, but expect approximately half of lookups to succeed. In the event of a failed lookup, MeSH and Google search linkouts are offered.



What are MeSH? Medical Subject Headings (MeSH) are terms defined by the National Library of Medicine as a way to organize and search the content of medical literature. In some ways, MeSH are similar to Nested Knowledge tags, but unlike tags, MeSH are standardized.

3. Topics

Explore topics that appear most frequently among the references. References may belong to one or more topics, or none. Clicking a topic shows references belonging to the topic.

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Create

Concept: Chronic Patients

Group:

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Concepts

Close

 Clozapine

Close

 Aripiprazole

Close

 Risperidone

Close

 Atypical Antipsychotics

Close

 Schizophrenia

Close

 Positive and Negative Syndrome Scale

Close

 Disability

Close

 Quality of Life

Close

 PANSS

Close

 Positive and Negative Syndrome Scale

Abstracts

RoboPICO

Topics

Keywords

Preview

Finalize

1 Clozapine

2 OR

3 Aripiprazole

4 OR

5 Risperidone

6 OR

7

1630 results

References By Topic

Title	Year
Insulin-like Growth Factor 2 (IGF-2) and Insulin-like Growth Factor Binding Protein 7 (IGFBP-7) Are Upregulated after Atypical Antipsychotics in Spanish Schizophrenia Patients.	2022
Interaction Testing and Polygenic Risk Scoring to Estimate the Association of Common Genetic Variants With Treatment Resistance in Schizophrenia.	2022
Pentoxifylline as an adjunctive in treatment of negative symptoms in chronic schizophrenia: A double-blind, randomized, placebo-controlled trial.	2023
The Role of Total White Blood Cell Count in Antipsychotic Treatment for Patients with Schizophrenia.	2023
Efficacy of Spironolactone as an Adjunctive Therapy to Risperidone to Improve Symptoms of Schizophrenia: A Double-Blind, Randomized, Placebo-Controlled, Clinical Trial.	2022
Factors influencing prolactin levels in chronic long-term hospitalized schizophrenic patients with co-morbid type 2 diabetes mellitus.	2022
Risperidone combination therapy with adalimumab for treatment of chronic	

These topics are derived from a [Carrot2](#) clustering of abstract text to identify semantically similar concepts and group them.

4. Keywords and N-Grams

Explore the frequency of word combinations (n-grams) from abstracts or indexed descriptors (MeSH and/or journal keywords). While n-grams are presented in order of occurrence in abstract text, descriptors are inherently unordered. Clicking a row shows unique references containing the combination.

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Schizophrenia

Intervention

Atypical Antipsychotics

Risperidone

Aripiprazole

Clozapine

Outcome

Quality of Life

Disability

Positive and Negative Syndrome S...

Positive and Negative Syndrome S...

Add a PICO element:

Type: Outcome

Negated

Element: Treated with Olanzapine

Add

Abstracts

RoboPICO

Topics

Keywords

PICO Detail

Query Builder

Keywords

Columns (N): 2

Keywords/MeSHs

Abstract n-grams

Rank	N-gram (1)	N-gram (2)	Frequency
1	Atypical	Antipsychotics	292
2	Quality	Life	265
3	Patients	Schizophrenia	113
4	Atypical	Antipsychotic	93
5	Rr	Ci	82
6	Negative	Symptoms	71
7	Long	Term	68
8	Adverse	Effects	67
9	Quality	Evidence	60
10	Antipsychotic	Drugs	57
11	Treatment	Schizophrenia	56
12	Low	Quality	51
13	N	Rr	47
14	Conventional	Antipsychotics	45

Associated References

Click a row to view associated references.

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Atypical Antipsychotics

Risperidone

Aripiprazole

Clozapine

Outcome

Quality of Life

Disability

Positive and Negative Syndrome S...

Add a PICO element:

Type

Outcome

Negated

Element

Treated with Olanzapine

Note

Add

Abstracts

RoboPICO

Topics

Keywords

PICO Detail

Query Builder

Columns (N):

2

Keywords/MeSHs

Abstract n-grams

Rank	Keyword (1)	Keyword (2)	Frequency
1	Antipsychotic Agents	Humans	156
2	Humans	Schizophrenia	146
3	Antipsychotic Agents	Schizophrenia	144
4	Humans	Quality Of Life	76
5	Antipsychotic Agents	Quality Of Life	75
6	Quality Of Life	Schizophrenia	73
7	Adult	Humans	71
8	Adult	Antipsychotic Agents	69
9	Female	Humans	65
10	Humans	Male	65
11	Antipsychotic Agents	Male	64
12	Adult	Schizophrenia	63
13	Antipsychotic Agents	Female	63
14	Female	Male	61

Associated References

Click a row to view associated references.

Next Steps

When is Search Exploration finished?

You should continue iteratively refining your query until your Abstract, RoboPICO, Topics, and/or Keywords contain mostly relevant content and minimal extraneous records or concepts.

It is useful to **check the total number of records** returned from your query. To do so, view the number of records in the bottom right of the Preview screen, where you can also click to view the query on PubMed:

Preview

Finalize >

1 (

2 Disability

3 OR

4 Severe

5 OR

6 Death

7 OR

6545 results

There is no 'right' number of records, but a good rule of thumb is to return:

1. A maximum of **200-300 records**, with
2. An anticipated inclusion rate **at or above 20%**.

The reasoning behind this recommendation is that you want to capture relevant records while minimizing extra work during Screening (remember, your team will need to manually Screen all results from your Search!). You can always add new/expanded Searches as you proceed, so achieving a high rate of inclusion should be prioritized over comprehensiveness.

What comes after Search Exploration?

When you are finished with Search Exploration, proceed to review, test, and finalize your search string in [Lit Search](#)!

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