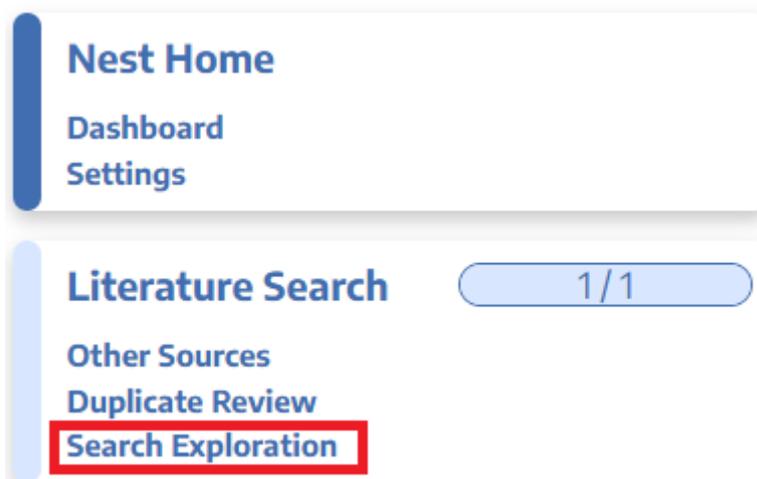


# Search Exploration

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.

The screenshot displays the 'Search Exploration' interface for the query 'Atypical Antipsychotics for Schizophrenia'. The interface is divided into several sections:

- Navigation:** Includes 'Nest Home', 'Literature Search', 'Screening', 'Tagging', 'Extraction', 'Study Inspector', and 'Synthesis'.
- Create:** A section for creating concepts, featuring a 'Group' box highlighted in red.
- Concepts:** A list of concepts including Clozapine, Aripiprazole, Risperidone, Atypical Antipsychotics, Schizophrenia, Positive and Negative Syndrome Scale, Disability, Quality of Life, PANSS, and Positive and Negative Syndrome Scale. A dropdown arrow is highlighted in red.
- Preview:** A section showing a list of concepts and a 'Finalize' button.
- Main Area:** Four bar charts showing the frequency of terms in different categories:
  - Population:** Shows terms like 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, and Medicare.
  - Intervention:** Shows terms like Risperidone, Olanzapine, Quetiapine, Clozapine, Antipsychotics, Aripiprazole, Haloperidol, Ziprasidone, Atypical, Placebo, Amisulpride, Chlorpromazine, Paliperidone, Flupenthixol, Antipsychotic, Blonanserin, Sertindole, Antipsychotic Drugs, Zotepine, Alctonine, Alctonine, Antipsychotic Therapy, Lais, Antiglucocorticoid, Antipsychotic Medication, and Antipsychotic Medications.
  - Outcome:** Shows terms like 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, and Quality.
  - Definition:** A section for viewing the MeSH Definition of a concept.

### 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.

The screenshot shows the 'Search Exploration' interface for 'Atypical Antipsychotics for Schizophrenia'. The 'Create' panel has a 'Concept' field with 'Type then "enter"' and a 'Group' field. The 'Concepts' panel lists several concepts: Intervention (Clozapine, Aripiprazole, Risperidone, Atypical Antipsychotics), Population (Schizophrenia), Outcome (Positive and Negative Syndrome Scale, Disability, Quality of Life), and a 'Drag & Drop' section. The 'Preview' panel shows a list of concepts: 1. Clozapine, 2. OR, 3. Aripiprazole, 4. OR, 5. Risperidone, 6. OR, 7. Atypical Antipsychotics, 8. AND, 9. Schizophrenia, 10. AND, 11. Positive and Negative Syndrome Scale, 12. OR, 13. Disability, 14. OR, 15. Quality of Life, 16. OR, 17. PANSS, 18. OR, 19. Positive and Negative Syndrome Scale. At the bottom, there are buttons for 'Refresh Exploration', 'Abstracts', 'RoboPICO', 'Topics', and 'Keywords'.

## 5. Run or Update Search Exploration

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

- Select the “Refresh Exploration” button

The screenshot shows the 'Search Exploration' interface after refreshing. The 'Refresh Exploration' button is highlighted with a red box. The 'Concepts' panel now includes 'Quality of Life' and 'PANSS'. Below the main panels, there are three bar charts: '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), '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), and '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). A 'Definition' panel is also visible on the right.

- 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.

Search Exploration: Atypical Antipsychotics for Schizophrenia

1/1

**Create**

Concept: Mortality

Group: Group

**Concepts**

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

Refresh Exploration

Abstracts RoboPICO Topics Keywords

PubMed

**Preview**

Finalize

1 ( Clozapine

2 OR

3 Aripiprazole

4 OR

5 Risperidone

6 1630 results

**Navigation**

Back Next

**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-naive 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.

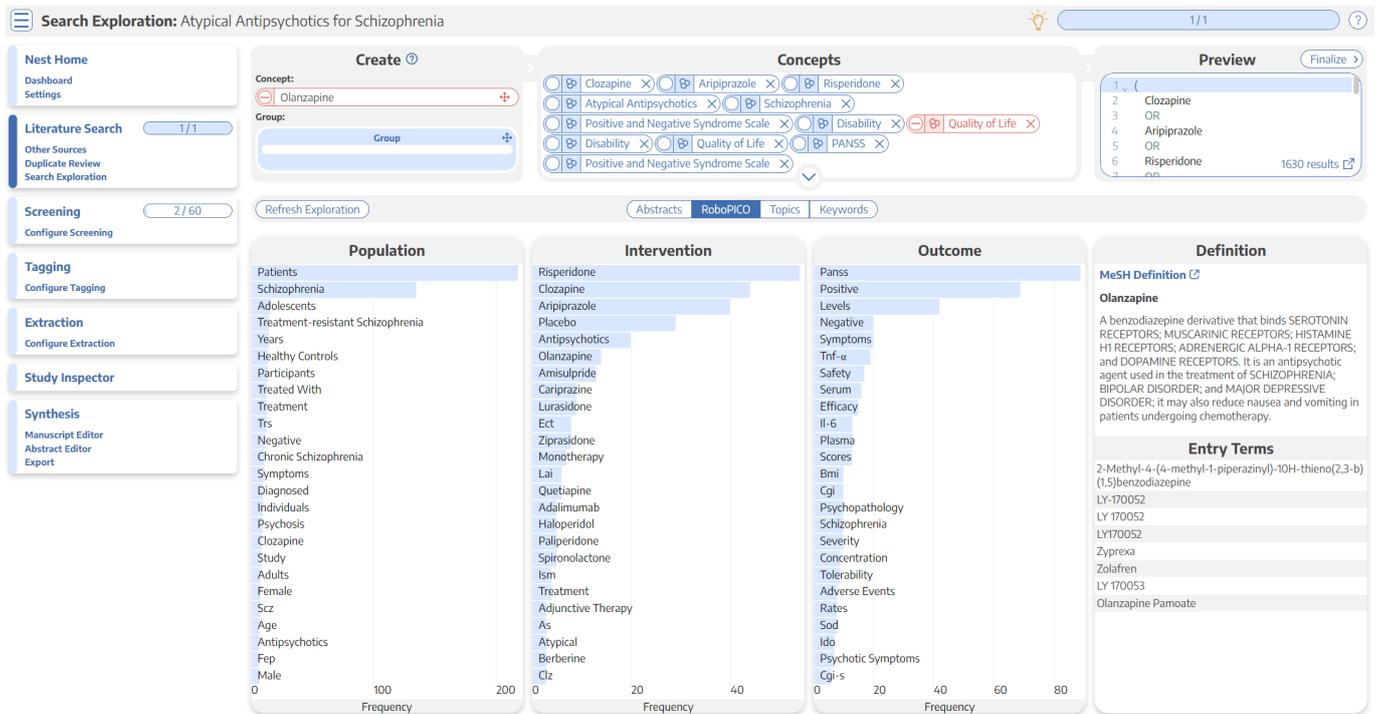
Population/Problem
  Intervention
  Outcome
  Your Keywords

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 clinical Populations, Interventions, and Outcomes with abstracts and titles. PICO elements are identified by RoboPICO, which is an open source fork of the models offered in RobotReviewer.



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 PICOs 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.

The screenshot displays the 'Search Exploration' interface for 'Atypical Antipsychotics for Schizophrenia'. It features a sidebar with navigation options like 'Nest Home', 'Literature Search', 'Screening', 'Tagging', 'Extraction', 'Study Inspector', and 'Synthesis'. The main area is divided into 'Create' (with 'Concept' and 'Group' fields), 'Concepts' (a list of terms like Clozapine, Aripiprazole, Risperidone, etc.), and 'Preview' (showing a list of results). Below these is a heatmap where rows represent patient groups (Chronic Patients, Psychosis Patients, Predict Response) and columns represent various concepts (Cognitive Functions, Placebo-controlled Trial, TRS Patients, Therapy with Risperidone, etc.). A 'References By Topic' table is also visible on the right, listing titles and years of relevant papers.

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.

Search Exploration: Atypical Antipsychotics for Schizophrenia

1/1

**Create**

Concept: Patients

Group: Group

**Concepts**

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

Refresh Exploration

Abstracts RoboPICO Topics **Keywords**

**Keywords**

Columns (N): 1

Keywords/MeSHs Abstract n-grams

Rank	N-gram (f)	Frequency
1	Patients	384
2	Schizophrenia	272
3	Treatment	264
4	PanSS	169
5	Symptoms	166
6	Negative	162
7	P	146
8	Study	131
9	Positive	130
10	Clozapine	124
11	Clinical	110
12	Scale	109
13	Group	103
14	Antipsychotic	90
15	Baseline	88
16	Significant	88

**Preview** Finalize

1 Clozapine  
2 OR  
3 Aripiprazole  
4 OR  
5 Risperidone  
6  
7  
1630 results

**Associated References**

Title	Year
The Impact of Antipsychotic Treatment on Neurological Soft Signs in Patients with Predominantly Negative Symptoms of Schizophrenia.	2022
Association Between Hippocampal Subfields and Clinical Symptoms of First-Episode and Drug Naïve Schizophrenia Patients During 12 Weeks of Risperidone Treatment.	2022
Impact of clozapine on disability and course of illness in patients with schizophrenia: A study from North India.	2021
Efficacy and safety of prophylactic use of benzhexol after risperidone treatment.	2023
Macroscale EEG characteristics in antipsychotic-naïve patients with first-episode psychosis and healthy controls.	2023
Early Antipsychotic Nonresponse as a Predictor of Nonresponse and Nonremission in Adolescents With Psychosis Treated With Aripiprazole or Quetiapine: Results From the TEA Trial.	2022
Long-term efficacy and safety of once-monthly Risperidone ISM® in the treatment of schizophrenia: Results from a 17-month open-label extension study.	2022

## 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 top right of the Preview screen, where you can also click to view the query on PubMed:

**Search Exploration: Atypical Antipsychotics for Schizophrenia**

**Concepts**

- Clonazepam
- Aripiprazole
- Risperidone
- Atypical Antipsychotics
- Schizophrenia
- Positive and Negative Syndrome Scale
- Disability
- Quality of Life
- PANSS

**Keywords**

Rank	Keyword (t)	Frequency
1	Schizophrenia	62
2	Humans	55
3	Antipsychotic Agents	47
4	Schizophrenia	28
5	Clonazepam	21
6	Treatment Outcome	19
7	Risperidone	19
8	Schizophrenia, Treatment-Resistant	11
9	Male	11
10	Female	10
11	Antipsychotics	9
12	Adult	9
13	Aripiprazole	9
14	Psychotic Disorders	9
15	Double-Blind Method	9
16	Psychiatric Status Rating Scales	8

**Preview**

```
1 (
2 Clozapine
3 OR
4 Aripiprazole
5 OR
6 Risperidone
7 OR
8 Atypical Antipsychotics
9 )
10 AND
11 (
12 Schizophrenia
13 )
14 AND
15 (
16 Positive and Negative Syndrome Scale
17 OR
18 Disability
19 OR
20 Disability
21 OR
22 Quality of Life
23 OR
24 PANSS
25 OR
26 Positive and Negative Syndrome Scale
27 NOT
28 (
29 Quality of Life
30 )
31 )
```

1630 results

To view the full query, expand using the dropdown arrow. You can view the results returned in PubMed by clicking on #### results. You can finalize the query (input it into your nest) by selecting Finalize and following the steps.

**Search Exploration: Atypical Antipsychotics for Schizophrenia**

**Concepts**

- Intervention**: Clozapine, Aripiprazole, Risperidone, Atypical Antipsychotics
- Population**: Schizophrenia
- Outcome**: Positive and Negative Syndrome Scale, Disability, Quality of Life, PANSS

**Preview**

```
1 (
2 Clozapine
3 OR
4 Aripiprazole
5 OR
6 Risperidone
7 OR
8 Atypical Antipsychotics
9 )
10 AND
11 (
12 Schizophrenia
13 )
14 AND
15 (
16 Positive and Negative Syndrome Scale
17 OR
18 Disability
19 OR
20 Disability
21 OR
22 Quality of Life
23 OR
24 PANSS
25 OR
26 Positive and Negative Syndrome Scale
27 NOT
28 (
29 Quality of Life
30 )
31 )
```

1630 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.

After hitting Finalize, you will be taken to the Add Search modal, but pre-populated with the query you have built. Here you can edit the query, the search engine, and notes before hitting Add. This adds the search just like a regular one!

### Create New Search

Automatic File Import

Query\* [Need help with your PubMed query?](#)

```
1 (
2 Clozapine
3 OR
4 Aripiprazole
5 OR
6 Risperidone
7 OR
8 Atypical Antipsychotics
9 )
10 AND
11 (
12 Schizophrenia
13 )
14 AND
15 (
16 Positive and Negative Syndrome Scale
17 OR
18 Positive and Negative Syndrome Scale
```

Search Engine\* PubMed

Note  
Enter your note

Schedule\* Never

Cancel This search will import 1637 results. **Add**

## 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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