## Critical Appraisal (previously named Risk of Bias)

## Objective

Evaluate the quality of evidence of included cohort studies or controlled trials.

## Configure Risk of Bias

From administrative settings, select the ROB mode.
Administrator Settings: Opioid Use Disorder - Phase I

## Risk of Bias

## Choose a system:

| No Selection |
| :--- |
| None |
| System: SIGN 50, Version: 2011 |
| System: Cochrane RoB, Version: 2 |
| System: JBI, Version: 2020 |

## Choose Scope

Assess Risk of Bias the study level or the outcome level:
Administrator Settings: Opioid Use Disorder - Phase I

Risk of Bias

Choose a system:
System: SIGN 50, Version: 2011

## Choose a scope:

Some systems allow you evaluate the risk of bias of entire studies or individual outcomes.

- Entire Study

Individual Outcomes

Select Outcomes:

| Data Element | Timepoint | RoB |
| :--- | :--- | :--- |
| \% Change employed | Outcome | $\square$ |
| \% abstinence | Outcome | $\square$ |
| \% change insured | Outcome | $\square$ |
| \% negative urine sample | Outcome | $\square$ |
| Anxiety | Outcome | $\square$ |
| cows Scale | Outcome | $\square$ |
| Confusion | Outcome | $\cap$ |

## Start Assessing Risk of Bias

## Navigate to ROB Module

After selecting the system and scope, reviewers can begin assessing ROB. You may need to refresh. Once the page reloads, ROB will appear in the navigation menu.

## Nest Home

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| :--- | :---: |
| Configure Screening |

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## Introduction

Acute ischemic stroke (AIS) is caused by embolic or thromboembolic occlusion of a cervical or cerebral artery. Until recently, AIS treatment focused on intravenous thrombolysis with tissue plasminogen activator (IV-tPA), and eligible patients could be treated within 3-4.5 h of symptom onset (1). More recently, multiple randomized clinical trials demonstrated that mechanical thrombectomy (MT) results in superior functional outcomes compared to standard medical therapy, which includes IV-tPA treatment (2-9). Moreover, MT may be offered to eligible patients up to 24 h after symptom onset, which has expanded treatment options for thousands of AIS patients.

Currently, patients who are eligible for both MT and IV-tPA are recommended to receive both treatments (10). However, the effectiveness of MT has raised the question of whether IV-tPA offers any additional benefit in the treatment of AIS patients who are eligible for both therapies.

The recently reported DIRECT-MT, SKIP, DEVT, and MR CLEAN NO IV trials randomized patients to either MT alone to MT+tPA, and each of these tria failed to identify a significant difference in functional outcomes between these two treatment strategies (11-14). In addition, it is not clear whether MT+tPA results in a higher frequency of vessel recanalization compared to MT alone (11-14). We hypothesized that these individual studies were underpowered to detect significant differences in recanalization rates and functional outcomes between MT+tPA and MT alone patients. Therefore, v performed a systematic review and meta-analysis to consolidate the findings of all eligible randomized controlled trials that address this comparison.

Traditional reviews and meta-analyses require researchers to manually identify relevant literature across multiple databases, a process which can be inefficient and unorganized. The data extraction process too requires manually standardizing the format of data, units, and time point definitions, wh lends itself to errors and can often be tedious (15). We sought to investigate a more streamlined approach, and thus performed this study using a nov semi-automated software platform (AutoLit, Nested Knowledge, Saint Paul, MN) that allows for the rapid identification, collation, synthesis, and analysis of data. Assessing the performance of this software platform was a secondary aim of this study.

## Methods

## Nested Knowledge Systemic Review Platform

A PRISMA and MOOSE-compliant systematic review of the literature was undertaken on the PubMed database through the Nested Knowledge (NK) platform (Supplementary Video 1) Prior to study selection and screening, two authors (G.A. and J.J.H.) established the framework for the study by writing up a protocol for the systematic review that included acceptable study designs, intervention arms, patient characteristics to collect as baselinf and outcome variables, as depicted in the NK sunburst diagram in Figure 1. These authors, also non-affiliates of NK, were also responsible for evaluating the functionality and efficiency of the NK platform as a secondary aim of this study.

## Read study and select study type

Depending on the selected ROB system, you may need to select a Cohort Study or Controlled Study to begin assessment.


## Assess study bias

Fill out the ROB questions as you read through the uploaded study.


Objective: Opioid use disorder (OUD) is associated with physical, Results: Participants receiving BUP-XR ( $\mathrm{n}=389$ ) versus placebo social, psychological, and economic burden. This analysis assessed ( $\mathrm{n}=98$ ) had significantly greater changes from baseline on the EQ $\begin{array}{ll}\begin{array}{l}\text { social, psychological, and economic burden. This analysis assesed } \\ \text { the effects of RBP-6000, referred to as BUP-XR (extended-recease }\end{array} & \begin{array}{l}5 \mathrm{D}-5 \mathrm{~L} \text { index ( } 300 / 300 \mathrm{mg} \text {. difference }=0.0636, P=0.003 \text { ), EQ-5D- } \\ 5 \mathrm{~L} \text { visual analog scale ( } 3001300 \mathrm{mg} \text { : difference }=5.9, P=0.017 \text {; }\end{array}\end{array}$ buprenorphine), a subcutaneously injected, monthly buprenorphine reatment for OUD compared with placebo on patient-centered atcomes measuring meaningful life changes. phase 3 , placebo-controlled study assessing the efficacy, safety and tolerability of BUP-XR $300 / 300 \mathrm{mg}(6 \times 300 \mathrm{mg})$ and $300 / 100 \mathrm{mg}$ ( $2 \times 300 \mathrm{mg}$ followed by $4 \times 100 \mathrm{mg}$ ) injections in treatment-seeking articipants with moderate-to-severe OUD. Measures included the $300 / 100 \mathrm{mg}$ : difference $=7.7, P=0.002$ ), and SF-36v2 physical component summary score $\quad(300 / 300 \mathrm{mg}$ : difference $=3.8$, $P<0.001 ; 300 / 100 \mathrm{mg}:$ difference $=3.2, P=0.002$ ). Satisfaction was significantly higher for participants receiving BUP-XR 300 $300 \mathrm{mg}(88 \%, P<0.001)$ and $300 / 100 \mathrm{mg}(88 \%, P<0.001)$ than increased by $10.8 \%$ and $4.1 \%$ with BUP-XR $300 / 300 \mathrm{mg}$ and $10.0 \%$ increased by $10.8 \%$ and $4.1 \%$ with BUP-XR $300 / 300 \mathrm{mg}$ and $10.0 \%$

You can monitor your progress, skip studies (and return to them later), and leave comments!
Note: Anytime there is a module box with the adjustable icon, you can drag to adjust the width of the box depending on your preference.


## Risk of Bias Visuals

By completing Risk of Bias, you automatically generate Risk of Bias visuals: Domain Distribution and Stoplight diagrams on Synthesis.

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