Comparison of Benzodiazepines Versus SSRIs in the Treatment of Panic Disorder With or Without Agoraphobia in Adults: A Systematic Review and Meta Analysis

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Abstract

Panic disorder is a fairly common anxiety disorder with a lifetime prevalence of about 3% in the United States. Untriggiered and persistent panic attacks, a short and extremely strong wave of panic, are its main symptom. While many treatments, both non-pharmacological and pharmacological, are used to treat this, the main medications prescribed are SSRIs (selective serotonin reuptake inhibitors) and benzodiazepines. This systematic review aims to determine and compare the effects of SSRIs and benzodiazepines on adults with panic disorder considering dropout rate, rate of remission, and adverse effects. A search of the electronic databases Science Direct, PubMed, PsycNet, and the Cochrane Database of Systematic Reviews (CDSR) was conducted from the year 2009 to December 2024. Three articles, one systematic review and two meta-analyses, were selected according to the eligibility criteria. Collectively, 766 patients were identified. After the systematic review was completed it was decided to conduct a standard inverse variance meta analysis, pooling the retrieved effect estimates. It was found that benzodiazepines have a significantly lower dropout rate while SSRIs have less adverse effects. However, SSRIs were also reported to have a slightly higher rate of remission, but the data was not statistically significant. While the statistics have shown that SSRIs are slightly superior to benzodiazepines, high risks of bias make it hard to make definitive conclusions. Until higher quality evidence is available, it is best that healthcare providers and patients choose the treatment best for the patient individually.

Keywords: systematic review, panic disorder, treatments, SSRIs, benzodiazepines

Introduction

Panic Disorder

Panic disorder (PD) is an anxiety disorder characterized by untriggered and unexpected panic attacks and a persistent fear of the attacks occurring again (*Panic Attacks and Panic Disorder - Symptoms and Causes*, n.d.). According to the DSM-5, panic disorder without agoraphobia has a lifetime prevalence of about 3% in the United States. Most often this disorder is diagnosed in the earlier stages of a person's life and if left untreated can negatively impact quality of life, leading to many future problems such as problems with socialization or developing of other disorders (*Panic Disorder: When Fear Overwhelms*, n.d.).

Causes of Panic Disorder

The prime symptom of PD, panic attacks, are usually not triggered in any way, and even now the exact causes are yet to be discovered (*Panic Attacks and Panic Disorder - Symptoms and Causes*, n.d.). It is important to note that it is possible to experience a panic attack due to a phobia or intense anxiety but in the case of panic disorder, the attacks are always seemingly untriggered. It is popularly believed that anxiety and mood disorders are caused by serotonin deficiencies, and while that is true, it is not the only cause (*Panic Attacks &Amp; Panic Disorder*, 2024). For panic disorder, there are several known risk factors that can make a person more likely to develop this disorder. First, researchers have found a trend showing that panic disorder has a major genetic factor. If a close relative has PD a person is about 40% more likely to develop this disorder. PD is also often comorbid with other mental disorders such as major depressive disorder. Finally, traumatic experiences have been found to contribute to the likelihood of panic disorder developing. Because of the mentioned risk factors it is likely that panic disorder has epigenetic components. It is possible that a problem with the functioning of the amygdala or with production of neurotransmitters is the cause of the condition itself, but it is still being investigated by researchers (Yoon et al., 2016).

Symptoms of Panic Attacks

Oftentimes patients experiencing an attack will confuse it with another health condition such as a heart attack due to the many similar physical symptoms and its unexpectedness. Those include the following:

- Rapid heartbeat
- Sweating
- Chills
- Shaking
- Difficulty breathing
- Fatigue or vertigo
- Tingling or numbness in nerve endings
- Chest pain

- Abdominal pain or nausea

(*Panic Disorder: When Fear Overwhelms*, n.d.)

A panic attack is described as a sudden and extremely strong wave of fear and a truly terrifying experience (*Panic Attacks and Panic Disorder - Symptoms and Causes*, n.d.). The panic will peak about ten minutes after the symptoms first begin and usually end soon after (*Panic Attacks &Amp; Panic Disorder*, 2024). During that time the person will feel as if they have lost all control or, in some cases, that they are dying (*Panic Disorder: When Fear Overwhelms*, n.d.).

Medication For Panic Disorder

While panic disorder can be treated with many different types of medication, SSRIs and benzodiazepines are the most common. Despite usually being an antidepressant used to treat depression and other mood disorders, SSRIs (selective serotonin reuptake inhibitors), can also be used for PD. Benzodiazepines (BZDs, benzos) are a commonly used type of anti-anxiety medications. Although they are able to mute the effects of panic disorder in a short amount of time, they are also quite easy to build a tolerance to, which can result in addiction and overdose. Usually the optimal medication is individual to the person. Not all medications for this type of disorder work the same for all people, and sometimes patients will need to try several different treatments to find the best one. If it is found that a medication is not working, the doctor may recommend a different medication or combination of treatments, such as psychotherapy and medication, to find an effective one. It is also important to note that most of the time significant improvements in the patient's mental health that will likely last will only be seen after a couple of weeks (*Panic Attacks and Panic Disorder - Symptoms and Causes*, n.d.).

How the Intervention Works

It is believed that the deficiency of serotonin (5-hydroxytryptamine/5HT) can partially be the cause of panic disorder. During neurotransmission, serotonin is first released from the presynaptic axon terminal into the synapses (synaptic gap/synaptic cleft). When the serotonin tries to be reuptaken into the presynaptic nerve, the SSRI inhibits that process, forcing the neurotransmitter to stay in the synapses. This means that serotonin will continue to be released into the synapses but it will no longer be able to be removed from there via reuptake, meaning that there chances of the neurotransmitter contacting and binding to its respective receptor on the postsynaptic nerve and stimulating is much increased (Chu & Wadhwa, n.d.). Thus, the brain is forced to use the serotonin it already has more efficiently, resulting in positive effects on mood and emotion (MSc, 2023).

Benzodiazepines work by interacting with the $GABA_A$ receptor and enhancing the properties of the gamma-aminobutyric acid, or GABA, neurotransmitter, which results in lowered anxiety and light sedation. GABA is the main inhibitory neurotransmitter in the CNS, which is thought to be responsible for reducing feelings of stress and anxiety. After GABA is released from the presynaptic nerve, it travels across the synapses and binds to the $GABA_A$ receptor (which is a channel-forming protein). The receptor then temporarily opens the channel to allow negatively charged molecules called chloride ions to go inside of the postsynaptic nerve (*Benzodiazepines: How Do They Work?*, n.d.). This lowers the cell's excitability, meaning that its ability to respond to stimuli through electrical impulses is slowed or

decreased (*Neuronal Excitability | the Human Brain*, n.d.). BZDs attach themselves to the benzodiazepine binding site on the $GABA_A$ receptor and stimulate it for longer, allowing more chloride ions to enter the cell. The result is the more than naturally possible depression or slowing of nerve impulses, meaning that nerve responses and general reaction time are severely decreased, thus the name central nervous system depressants (*Benzodiazepines: How Do They Work?*, n.d.)

Objective

The objective of this review is to compare the effects of SSRIs and benzodiazepines on adults with panic disorder, particularly:

1. to determine which of the two is more effective in treating panic disorder with or without agoraphobia using the rate of remission as a scale;
2. to measure the total amount of dropouts in both groups due to any reason and use it as a proxy measure of acceptability; and
3. to determine and compare the amount of adverse effects for SSRIs and benzodiazepines.

Method

Eligibility Criteria

Types of Studies

Studies such as double-blind randomised controlled trials (RCTs), meta-analysis, and systematic reviews written and conducted in the last 15 years (as of December 2024) addressing at least one of the following topics of interest: dropout rate, rate of remission, and measures of adverse effects. The studies had to directly compare benzodiazepines and SSRIs for the treatment of panic disorder and had to have 25 or more participants. Any studies that did not have free or easily accessible full text versions or were not written in English were excluded. The studies in this review meet all of the listed criteria.

Participants

Participants had to be officially diagnosed with panic disorder, over 18 years of age, and have no serious physical or psychiatric comorbidities. Unfortunately, due to the lack of studies and its common presence in patients with panic disorder, studies with patients with comorbid agoraphobia were included in this review.

Search Strategy

A search of the following four electronic databases was conducted: Science Direct, PubMed, PsycNet, and the Cochrane Database of Systematic Reviews (CDSR). A filter was set to exclude studies published more than 15 years before the day that the search was conducted (1 December, 2024). The keywords “panic disorder” AND “benzodiazepine” AND “SSRI” were used, however the search was altered and other keywords were used in place. “Benzodiazepines” was used in place of “benzodiazepine”

and “SSRIs” in place of “SSRI”. The specific medication names were also replaced by “pharmacological” AND “treatments” or just “treatment” to obtain broader results. The first search terms were used the most. The search was conducted by one independent researcher and PRISMA guidelines were used.

Synthesis Methods

After the search was completed, data that reported outcomes of interest were extracted. This was done manually by one independent researcher. Of the three included studies only Chawla et al. (2022) clearly reported all measured outcomes, while the others presented results differently, requiring the data to be converted. While Bighelli et al. (2016) reported on all three outcomes of interest, the comparison was between SSRIs and benzodiazepines rather than benzodiazepines and SSRIs, which was the format the rest of the studies presented their outcomes. For that reason, all three of the statistical summaries (risk ratios and confidence intervals) that were being used in this review from Bighelli et al. (2016) had to be “flipped”. This was done according to the formula which states that the inverted risk ratio can be found by dividing one by the risk ratio; in other words the inverted risk ratio is the reciprocal of the original risk ratio. Same goes for the upper limit (UL) and lower limit (LL) of the confidence interval. The flipped upper limit is the reciprocal of the lower limit and vice versa.

$$RR_{flipped} = {}^{1}/_{RR}$$

$$LL_{flipped} = {}^{1}/_{UL}$$

$$UL_{flipped} = {}^{1}/_{LL}$$

(Figure 1)

Additionally, while Bighelli et al. (2016) reported on remission and adverse effects, they presented two out of the three outcomes in a negative way (failure to remit and which treatment has a higher number of adverse effects) despite the preferred reporting method of this data for this review being a positive presentation (rate of remission and which treatment has a lower number of adverse effects). To convert the negative presentation to a positive, the same formula as previously used to flip the comparisons was used. This resulted in the twice adjusted risk ratios and confidence intervals to be the same as their respective originals.

Finally, Guaiana et al. (2023) reported their results in the Baysian method rather than the frequentist like all other studies in this review (uses credible interval instead of confidence interval, etc.). This made the creation of graphs difficult as there is no direct conversion between them. It was decided to include a separate section for results from Guaiana et al. (2023) into the graphs or presented it in a narrative format as seen below in Table 3. The original and adjusted results can be seen in Tables 2 and 3 respectively.

Study Name	Outcomes		
	Dropout Rate	Remission	Adverse Effects
Bighelli et al. (2016)	(RR 1.71, 95% CI 1.03 to 2.84) SSRIs vs BZDs	*Failed to remit (RR 1.12, 95% CI 0.79 to 1.59) SSRIs vs BZDs	(RR 1.03, 95% CI 0.92 to 1.15) SSRIs vs BZDs
Chawla et al. (2022)	(RR 0.51, 95%CI 0.38 to 0.67) BZDs vs SSRIs	(RR 1.07, 95% CI 0.96 to 1.19) BZDs vs SSRIs	(RR 1.47, 95% CI 1.18 to 1.84) BZDs vs SSRIs
Guaiana et al. (2023)	(RR 0.62, 95% Crl 0.44 to 0.83) BZDs vs SSRIs	-	-

(Table 1) Raw data

Study Name	Outcomes (Risk Ratios and Confidence Intervals)		
	Dropout Rate	Remission	Adverse Effects
Bighelli et al. (2016)	(RR 0.58 95% CI 0.35 to 0.97) BZDs vs SSRIs	(RR 1.12, 95% CI 0.79 to 1.59) BZDs vs SSRIs	(RR 1.03, 95% CI 0.92 to 1.15) BZDs vs SSRIs
Chawla et al. (2022)	(RR 0.51, 95%CI 0.38 to 0.67) BZDs vs SSRIs	(RR 1.07, 95% CI 0.96 to 1.19) BZDs vs SSRIs	(RR 1.47, 95% CI 1.18 to 1.84) BZDs vs SSRIs

(Table 2) Adjusted Data. Guaiana et al. (2023) reported a Bayesian risk ratio of 0.62 and credible intervals (Crl) of 0.44 to 0.83.

Data Management

Dichotomous Data

All data gathered was found to be dichotomous (binary), using risk ratios (RR) and with corresponding 95% confidence intervals (CIs). It was decided that it was not to convert to odds ratio (OR) as they are generally considered more difficult to understand than risk ratios (Grimes & Schulz, 2008). For these reasons it was not necessary to estimate risk ratios or any other type of statistical summaries before conducting the meta analysis.

Missing and Insufficient Data

Fortunately, no missing data was identified for the observed outcomes, however this presented itself with other challenges. Within the two syntheses included in this meta analysis, there were only three smaller studies (all randomised controlled trials), one in Bighelli et al. (2016) and two in Chawla et al. (2022). This created a number of problems, as it meant that while the pooled effect estimates would be more accurate, it still wouldn't be able to accurately portray the situation outside of the conducted clinical trials.

Data Synthesis

After the initial completion of the systematic review, it was decided that a meta analysis was able to be conducted. However, it is worth noting that Guaiana et al. (2023) was excluded from the meta-analysis as it is a study done in Bayesian statistics, rather than the preferred frequentist. A standard inverse variance meta-analysis was conducted, using a fixed-effects model for the first two observed outcomes (dropout rate and remission) and a random-effects model for the last (adverse effects). This was done because the results from both studies of the first two outcomes were extremely similar, alluding to a similar true effect and low heterogeneity. In the final outcome of adverse effects a large difference between the reported results was observed. As previously mentioned, it was decided to use a random-effects model due to the fact that it better accounts for the variation that was present, creating a more accurate representation of the effect of the intervention.

It was determined that the statistical software R would be the best tool to conduct this meta-analysis. The software uses the same-named programming language, however due to its rarity and scarce applications elsewhere, we were not familiar with this language. For this reason it was decided to use a generative artificial intelligence to create code that would do the desired function. However, it is important to note that the created code was not perfect and contained example data only. It had to be manually adjusted and the retrieved results from included studies were also entered by hand. Additionally, the generative artificial intelligence did not conduct the meta-analysis nor did it receive or interpret the results. The code was exported to the previously mentioned statistical software R where the analysis was conducted and data was extracted for interpretation. This was done manually by one independent researcher.

Heterogeneity

As per the Cochrane Handbook of Systematic Reviews of interventions, heterogeneity is to be qualified using I^2 (based on Cochran's Q) and Chi^2, along with its p-value. Heterogeneity was interpreted as the following:

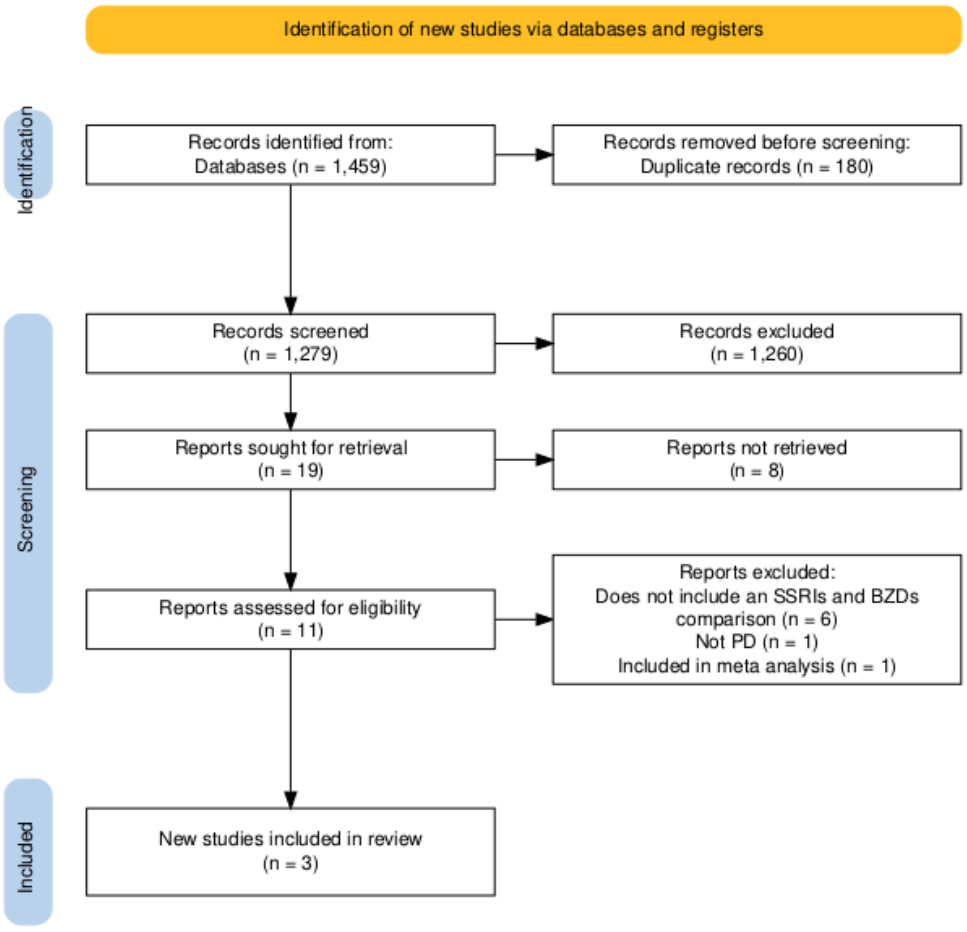
1. 0% to 40%: might not be important;
2. 30% to 60%: may represent moderate heterogeneity;
3. 50% to 90%: may represent substantial heterogeneity;
4. 75% to 100%: considerable heterogeneity.

The conventional threshold of ≤0.05 for the p-value of Chi^2 was used to indicate statistically significant results. Unfortunately, due to the low number of studies included in the meta-analysis, meta regression and subgroup analyses were not able to be conducted. The results would have been unreliable as there would have been more parameters that accounted for the heterogeneity than data points present.

Results

Screening and Selection Process

A total of 1459 studies were identified and exported to Endnote Basic. Using the program's duplicate remover 180 duplicates were removed. The remaining 1279 studies' titles and abstracts were screened and 1260 were excluded. The remaining 19 were to be retrieved for full-text screening but unfortunately 8 weren't because their full-text versions were not accessible. Finally, 11 studies were assessed for eligibility with 8 of them being excluded. Six of them because they did not contain a direct and clear comparison between SSRIs and benzodiazepines, one because it did not focus on panic disorder, and the last one was excluded because it was a RCT within a meta analysis that was included in this review. Studies deemed similar by the databases were also screened. Therefore, this review includes two meta-analyses and one systematic review (Figure 2). The screening and selection process was conducted by one independent researcher.



(Figure 2)

Characteristics of Included Studies

From the three included studies a total of 766 participants have been identified. Unfortunately, Guaiana et al. (2023) did not specify how many participants were in each group, meaning that exact number of patients being treated with SSRIs or benzodiazepines is unknown. Additionally, the two meta-analyses (Guaiana et al. (2023) and Chawla et al. (2022)) did not specify the age of participants, besides quote "All participants were over the age of 18" or "the participants were adult". All three reviews had an unspecified number of participants with agoraphobia. Other characteristics are shown in Table 3.

Author	Study Type	Published	Agoraphobia	Group	Sample Size	Age (years ± SD)
Bighelli, I	Systematic Review	2016	Some	SSRIs	77	39.1 ± 11.1
				BZDs	77	39.5 ± 12.5
Chawla, N.	Systematic Review and Network Meta-Analysis	2022	Some	SSRIs	77	NA
				BZDs	83	NA
Guaiana, G.	Network Meta-Analysis	2023	Some	SSRIs	452	NA
				BZDs		NA

(Tabel 3)

Effects of Intervention

The only outcome assessed and reported by all three studies was dropout rate of benzodiazepines compared to SSRIs. All reported results were similar and statistically significant, with little variation and showing a clear trend. Bighelli et al. (2016) reported a risk ratio of 0.58 with a 95% confidence interval of 0.35 to 0.97, indicating statistical significance. The two meta-analyses (Chawla et al. and Guaiana et al.) showed similar results. A risk ratio of 0.51 and a 95% confidence interval of 0.38 to 0.67 were reported by Chawla et al. (2022). Guaiana et al. (2023), being a study done in Bayesian statistics, cannot have its results interpreted in the exact same way as the other two studies. Nonetheless, the study showed conclusive results of RR 0.62, 95% CrI (credible interval) 0.44 to 0.83. Overall, all studies reported, with statistical significance, that benzodiazepines have a significantly lower dropout rate than SSRIs.

Study Name	Risk Ratio	Confidence Interval (95%)
Bighelli et al. (2016)	0.58	0.35 to 0.97
Chawla et al. (2022)	0.51	0.38 to 0.67
Study Name	**Risk Ratio**	**Credible Interval (95%)**
Guaiana et al. (2023)	0.62	0.44 to 0.83

(Table 4) Dropout rate, benzodiazepines versus SSRIs

Unfortunately, the remission outcome was only measured by two studies, Bighelli et al. (2016) and Chawla et al. (2022). The studies were once again in agreement with each other, the reported results however, cannot be considered statistically significant as the lower limit crossed one in both cases. Bighelli et al. (2016) observed a slightly higher chance of remission in the SSRI group compared to the benzodiazepine group, presenting a risk ratio of 1.12 and a 95% confidence interval of 0.79 to 1.59. Chawla et al. (2022) showed a risk ratio slightly lower than the systematic review: RR 1.07, 95% CI 0.96 to 1.19. While the results were consistent, with SSRI having a higher remission rate, the data was not statistically significant.

Study Name	Risk Ratio	Confidence Interval (95%)
Bighelli et al. (2016)	1.12	0.79 to 1.59
Chawla et al. (2022)	1.07	0.96 to 1.19

(Table 5) Remission rate, benzodiazepines versus SSRIs

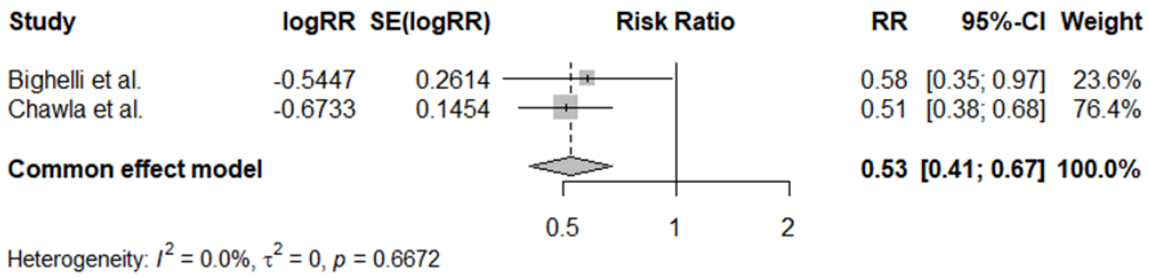
Finally, adverse effects were measured in the same studies that reported on the previous outcome, Bighelli et al. (2016) and Chawla et al. (2022). The results here differed significantly. Bighelli et al. (2016) reported that benzodiazepines and SSRIs have almost the same amount of adverse effects (RR 1.03 95% CI 0.92 to 1.15) with no statistical significance. On the other hand, Chawla et al. (2022) showed that SSRIs have a significantly lower amount of adverse effects compared to benzodiazepines with a risk ratio of 1.47 and a 95% confidence interval of 1.18 to 1.84. While it was observed that SSRIs have less adverse effects, there is quite the large difference in the reported statistics, making it more difficult to make accurate conclusions.

Study Name	Risk Ratio	Confidence Interval (95%)
Bighelli et al. (2016)	1.03	0.92 to 1.15
Chawla et al. (2022)	1.47	1.18 to 1.84

(Table 6) Adverse effects, benzodiazepines versus SSRIs

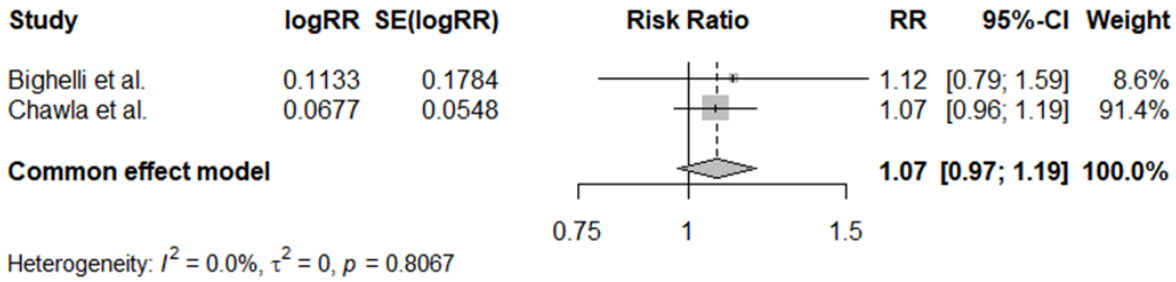
Pooled Effects of Intervention

In the outcome of dropout rate, due to the smaller range between the lower and upper confidence intervals, Chawla et al. (2022) had a greater weight in this outcome. This resulted in the pooled risk ratio estimate of a 0.53 risk ratio and a 95% confidence interval from 0.41 to 0.67 to be slightly closer to that of Chawla et al. (2022)'s original estimate, rather than Bighelli et al. (2016)'s. No heterogeneity or variance was found, and the Z-test's p-value was < 0.0001, significantly lower than the established threshold of less or equal to 0.05 for statistical significance. This indicates that benzodiazepines have a significantly lower dropout rate than SSRIs, with statistical significance. Guaiana et al. (2023), while excluded from the meta analysis, reported a risk ratio of 0.62, with a 95% credible interval of 0.44 to 0.83, further backing the meta-analysis results.



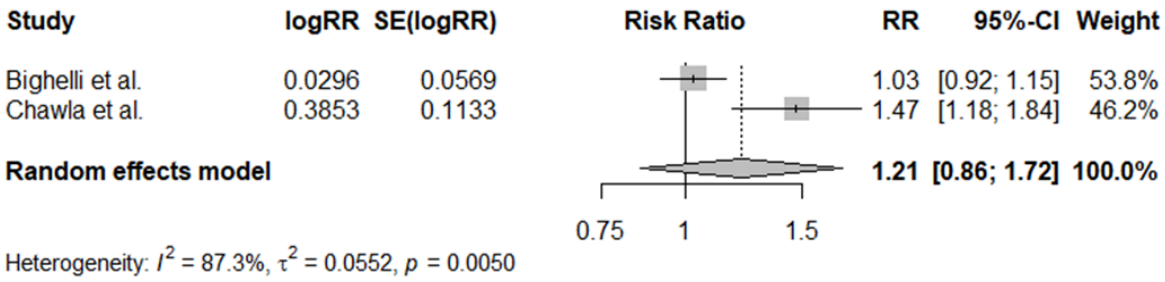
(Figure 3) Pooled dropout rate, benzodiazepines versus SSRIs

The pooled effect estimate for the outcome of remission is the most definitive out of the three. While the risk ratio of 1.07 and a 95% confidence interval of 0.97 to 1.19 is quite conclusive, it cannot be considered statistically significant. The p-value of 0.1717 paired together with the results, indicates that despite the fact that SSRIs are most likely to be favoured in the outcome of remission, the true effect size may favour either treatment. However, there was once again no heterogeneity. Thus, it was observed that the results were consistent, with SSRI having a slight advantage, the data was not statistically significant.



(Figure 4) Pooled remission rate, benzodiazepines versus SSRIs

As expected, an extremely high amount of heterogeneity and variance was observed in the outcome of adverse effects. The result from I^2 was 87.3%, which according to the predefined scale indicates considerable heterogeneity. The pooled risk ratio itself is 1.21 with a 95% confidence interval of 0.86 to 1.72. Because of the large amount of heterogeneity and a random effects model being used to calculate the pooled effect size, the upper and lower limits of the confidence intervals are extremely far apart. For that same reason, the p-value was quite high as well (0.2742). From this we can conclude that while SSRIs seem to have less adverse effects, the results weren't consistent or statistically significant, making it hard to draw accurate conclusions.



(Figure 5) Pooled adverse effects, benzodiazepines versus SSRIs

Bias in Studies Included in Syntheses

While a bias assessment of the included syntheses was not conducted, we analysed the assessments that were provided by them of their included studies. The study included in Bighelli et al. (2016) was funded by the pharmaceutical company GSK, therefore having a high risk of other bias according to the GRADE risk assessment tool used. The smaller study was also at an unclear risk of selection bias, performance bias, and detection bias, but at a low risk of attrition bias and reporting bias. The systematic review also mentioned that only unpublished data from this study was used, providing no further information. Chawla et al. (2022) stated that "Most of the studies had at least some concerns (70%; 61/87 [from total studies]) or were at high risk of bias (29%; 25/87 [from total studies])". They also said that most bias was caused by lack of details in the "randomisation and concealment processes". The study used the Cochrane risk of bias tool for randomised trials (RoB 2.0). Finally, Guaiana et al. (2023) used both RoB 2.0 and GRADE for bias assessment, saying that most studies had either an unclear or high risk of bias due to sources of support and funding. However, they did not separately list the individual studies used in each comparison, so we were not able to find the characteristics and assessment of the studies included in the observed outcome.

Discussion

SSRIs and benzodiazepines have been battling to be the best pharmacological treatment for panic disorder for many years. Unnecessary and untrue bias was expressed towards both treatments with little evidence to support the claims. However, this paper has demonstrated that while SSRIs likely have less adverse effects, benzodiazepines have significantly less dropouts. A possible reason as to why this was observed is that patients are able to see results faster, making them think that the treatment is especially effective. While that inference would not be entirely accurate, it may raise the patient's morale, improving their overall wellbeing. From this we can conclude that benzodiazepines are more acceptable in the treatment of panic disorder, as patients are willing to potentially tolerate more adverse effects for faster results. The results for remission however, were inconclusive. While SSRIs performed slightly better in both included studies and the meta-analysis, the p-value was higher than the established threshold, indicating statistical insignificance.

This review brought together and compared pooled risk ratios and confidence intervals from three different studies to determine and interpret any found trends or patterns. Afterward, by conducting a meta analysis, combining results from several syntheses, we were able to get the most holistic and comprehensive view on this subject. Only studies which were published less than 15 years ago were included to ensure that false impressions and inferences would not be present due to insufficient understanding of the effects of psychotropic medications on the human central nervous system. Despite these strengths, this review has many limitations. The main ones were the bias present in the studies included in the syntheses and the small sample size. All studies had some kind of bias present, which can easily lead to false data and conclusions. This would explain the large gap between the data reported by Bighelli et al. (2016) and Chawla et al. (2022) in the outcome of adverse effects. The limited number of included studies may have resulted in a narrowed impression and data that would not be applicable in clinical situations. Additionally, none of the studies reported on rate of relapse or other long-term outcomes that could have shown whether treatments have lasting effects enough to make improvements in the patients' lives. Finally, the reviews all had slight differences in their eligibility criteria, particularly the comorbidities section. Different combinations of mental or physical disorders can result in being less responsive to treatment or other nuances that could have caused skewed data. It was also possible, though unlikely, that errors have been made during the data synthesis process resulting in slight inaccuracies.

Benzodiazepines and SSRIs are two of the best treatments that could be offered at this time, but gene therapy for panic disorder, while not yet achievable, could be an option in the future due to the disorder's epigenetic components. However, in the near future it may be more plausible to observe the long term outcomes of both treatments such as relapse and patient satisfaction or the efficacy of combined psychotherapy and medication treatment. This could provide both healthcare professionals and patients with more accurate and relevant information on the effects of benzodiazepines and SSRIs in the treatment of panic disorder. Further exploring combined or non-pharmacological treatments that were previously mentioned could help us better understand human brain function and reduce patients' exposure to risks. It has been known that benzodiazepines have many associated dangers, meaning that reconsidering them as a primary treatment for panic disorder could significantly benefit patients. This review attempted to find

the superior pharmacological treatment of panic disorder, and while evidence was found and conclusions were drawn, a lot more work needs to be done. The amount of bias found shows that more high quality studies are needed to allow for better conclusions and the small sample size could provide a limited view. Nevertheless, this review managed to confirm and solidify SSRIs as the slightly better treatment for panic disorder.

Conclusion

According to the data gathered in this review, benzodiazepines and SSRIs would both be acceptable treatments of panic disorder as they each did better than the other in two of the measured outcomes (dropout for benzodiazepines and adverse effects for SSRIs) and performed similarly in the third (remission). While the statistics have shown that SSRIs are slightly superior to benzodiazepines, some of the results were inconclusive. Furthermore, studies noted a high risk of bias which could result in selective reporting or inaccurate data. In the future, more quality evidence could help us make a more definitive conclusion, but until then the choice of medication should be made by the patient and the healthcare provider to ensure that the patient gets the treatment that works best for them.

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