

What is the untreated remission or natural recovery rate of people with depression? A systematic review and meta-analysis

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Abstract: The aim of this study was to estimate the remission (natural recovery) from untreated depression. We systematically searched EMBASE, PsycINFO, and PubMed supplemented with additional relevant sources to identify studies reporting natural recovery from untreated depression. Screening and data extraction were carried out by three independent reviewers. The data were synthesized using random-effects meta-analysis. We included 16 studies in this systematic review and meta-analysis. Most of the included studies were randomized waitlist control trials. The overall pooled remission from untreated depression was 22.6% with widely varied follow-up duration ranged from one month to six years. The remission was 11.4% within three months of follow-up period and 49.2% within six months or more duration. Remission within short untreated period is not common where 1 in 10 people may remitted within 3 months duration of untreated depression. Interpretation of the result should be considered in caution as the data from waitlist controls may represent mild-to-moderate depression.

Keywords: Spontaneous remission; Natural recovery; Untreated depression

1. Introduction

Depression is a common illness and leading cause of disease burden globally [1,2]. However, most cases of depression did not get treatment [3]. A community based survey from 15 countries reported that every 2 in 5 depression cases received any mental health service and the gap for effective treatment is as high as 90% [4]. Many barriers contribute to hinder people with depression to access treatment [5] and the perceived urgency of treatment planners could be diminished [6] due to spontaneous remission of some depression cases [7].

Understanding the outcomes of depression is critical due to the chronic and recurrence nature of the illness. Depression can be treated effectively [8,9]; up to 60% can achieve stable recovery and 70 – 85% may recovered at least once during their follow-up [10]. This recovery rate includes both treated and untreated depression. Treatment delay and longer duration of untreated depression can decrease this recovery rate, increase the risk of worse outcomes, and prolong illness duration [11]. In some cases, however, particularly in mild-to-moderate depression, remission may occur without treatment [7,12].

As a significant number of people ($\approx 5\%$) fulfilled criteria for depression in a year [2,3], it will be challenging to achieve 100% treatment coverage [7]. Estimating the proportion of depression cases remitted without treatment will help the policymakers to plan the urgent treatment target. It is also helpful for clinicians to consider a short watchful period before initiating active treatment for mild-to-moderate depression. Therefore, the objective of this systematic review and meta-analysis was to estimate the remission rates for untreated depression.

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2. Methods

This Systematic review was conducted in accordance with PRISMA guidelines and registered on PROSPERO, [CRD42020198773](https://www.crd42020198773).

2.1. Eligibility criteria

Studies were included if they were: 1) samples of people with depression, including depressive disorder, major depressive disorder, major depressive episode, depression assessed and categorized based on a validated measurement tool; 2) untreated, i.e. not exposed to treatment for their depression, including samples of participants on wait-list or natural cohorts who had not accessed treatment. Studies comparing the effects of intervention versus placebo for the treatment of depression were excluded because placebo is not classified as untreated in this review; 3) reported on the proportion of remission, i.e. the percentage of participants with rescinded diagnosis or no longer in the depressed category at given a certain time period. The review considered peer-reviewed papers in English issued from 2010 onwards to capture current evidence.

2.2. Search strategy

Databases searched included EMBASE, PsycINFO, and PubMed. Dates of coverage were 2010-01-01 to, the date of the search, 2020-07-20 to capture publications in the past 10 years. Supplementary sources included hand searches through PROSPERO, Google scholar, and secondary references of relevant papers.

We used a two-step approach to identify studies for inclusion. First, we systematically searched for existing reviews and screened the original studies included in relevant reviews identified to collect potential articles for inclusion. We then conducted a search for original studies. We did a title or abstract or MeSH Term search for studies using synonyms and related terms for the concept "Depression AND Untreated AND Remission". Limits applied were: Language: English AND Year: 2010 onwards, in accordance with our eligibility criteria.

2.3. Study selection and data extraction

Study selection and screening were carried out by three independent reviewers of this review. Conflicts were resolved by discussion and review against inclusion criteria. Independent reviewers extracted the data using a standardized data extraction form. Data were extracted on study details (study design, year of publication, country), participants characteristics (inclusion criteria, mean age, female proportion, sample size), and outcome details (assessment tool, the definition of remission, and proportion of untreated remission).

2.4. Quality assessment

The methodological qualities of the included studies were evaluated using a templet from existing review [7]. This templet assesses the quality of the studies based on the sampling method, diagnostic assessment, untreated status of samples, definition of remission, and response rate.

2.5. Synthesis of results

We estimated the proportion of remission from untreated depression by the random-effects model meta-analysis using DerSimonian and Laird method [13]. The variance of proportions was stabilized using Freeman-Tukey double arcsine transformation. Heterogeneity was assessed using the I^2 statistics. We assessed the publication bias using the funnel plots and egger's test. Subgroup analysis was conducted by the duration of follow-up. All analyses were done using Stata version 16 (Stata Corporation, USA).

3. Results

3.1. Study characteristics

We identified 57 studies eligible for full text assessment and 16 studies were included in the narrative review and meta-analysis (Fig. 1). All the included studies were from high-income countries, involved 1422 untreated participants with depression. From the 16 studies, 12 studies were waitlist control trials [14-25] and 4 studies were follow-up studies [26-29]. Studies were from community-based samples (n=5), clinical settings (n=5), internet based (n=4), and school based (n=2). The quality of studies ranged from 25 – 100%.

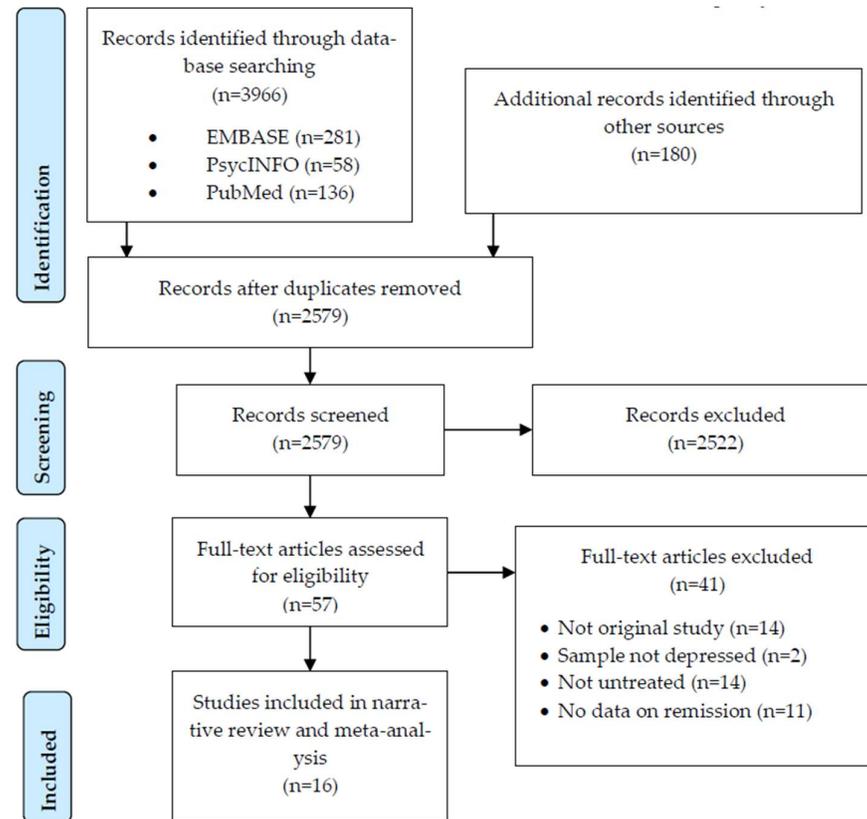


Figure 1. PRISMA flowchart for the search for original studies on remission among people with untreated depression.

3.2. Remission from untreated depression

The pooled estimate showed that the overall remission from untreated depression was 22.6% (11.9, 35.2%) with significant between studies heterogeneity ($I^2 = 95\%$, $p < 0.001$). Subgroup analysis by duration indicated that remission from untreated depression was 11.4% within 3 months and 49.2% within 6 months and above (Fig 2). The funnel plot is slightly asymmetric that shows few studies were missed in the right side. However, Egger's test ($p=0.095$) indicated no small study effect.

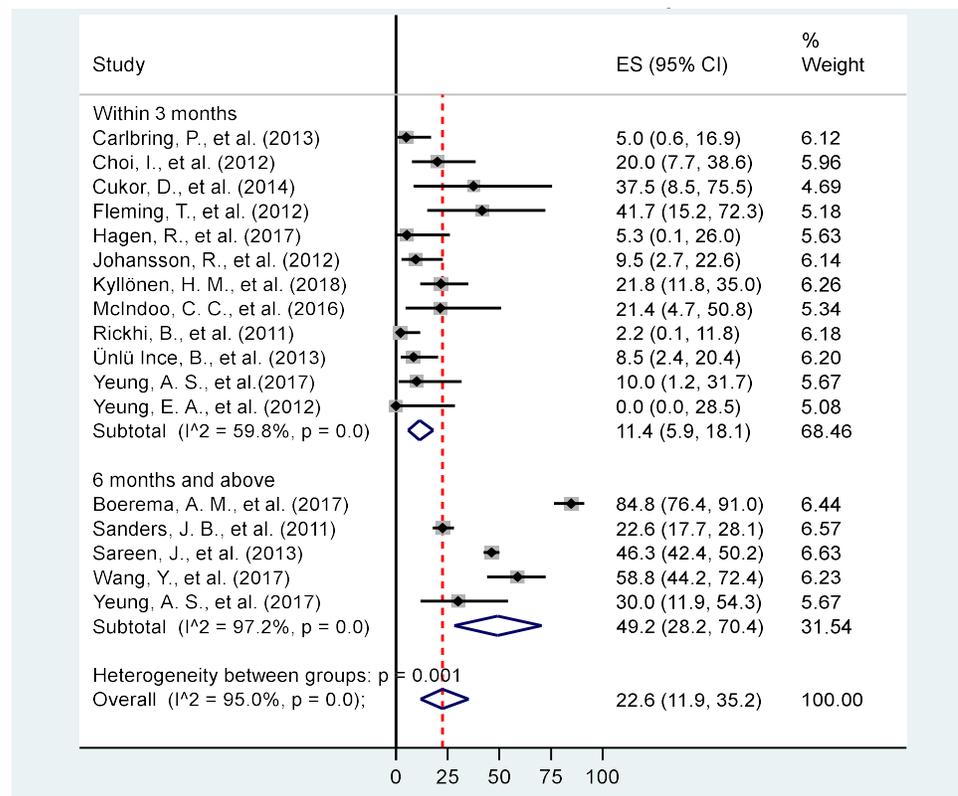


Figure 2. Remission from untreated depression by duration (forest plot).

4. Discussion and conclusion

This systematic review and meta-analysis involved 1422 untreated cases of depression in high-income countries. We did not find studies reporting remission from untreated depression in low- and middle-income countries. The pooled remission rate from untreated depression was 22.6%. We reported substantial between studies heterogeneity which might limit the generalizability of our findings. The duration for untreated follow-up period widely varied from 1 month to 6 years. We found that 11.4% of untreated depression cases achieved remission within 3 months. This is lower than a previous review that reported 23% of spontaneous remission within 3 months [7]. In studies that conducted 6 months or longer follow-up, nearly half (49.2%) of untreated depression cases remitted. This is in line with the previous review that reported 53% untreated remission within 1 year [7]. As the course and prognosis of depression varies and unpredictable [30], some of the patients remit without treatment while considerable number of cases did not improve even with treatment [31]. Though effective interventions are available, it is not clear yet to predict who will be most benefited from a specific intervention [31]. It might be plausible for clinicians to consider a short observational period for mild-to-moderate depressive symptoms before initiating active treatment.

This systematic review and meta-analysis mostly represent mild-to-moderate depression as most (75%) of the included studies were from waitlist-control groups. This is also the case in the previous Whiteford et al review [7]. Most of the included studies in our review did not involve severe depression or excluded participants with suicidal ideation which may indicate severe cases. Hence, our findings of remission rate from untreated depression may not infer severe cases of depression.

Conflicts of Interests: None

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