TIP RESEARCH LAB
Therapeutic Interventions For Psychosis

UNIVERSITY OF TORONTO

CIHR KNOWLEDGE SYNTHESIS: EXAMINING THE EFFICACY OF EVIDENCE-BASED PSYCHOSOCIAL INTERVENTIONS FOR SCHIZOPHRENIA-SPECTRUM DISORDERS DELIVERED THROUGH VIRTUAL CARE

June 22, 2020*

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*Disclaimer: The results presented herein are representative of work conducted up until June 22, 2020. These results may change with further examination of the literature and should not be considered as a final definitive review of the literature at this time.

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EXECUTIVE SUMMARY

Background: Schizophrenia-spectrum disorders are among the most persistent and debilitating mental illnesses worldwide, and most treatment options are delivered in person. Individuals with severe mental illnesses such as schizophrenia-spectrum disorders are projected to be among the most affected by the COVID-19 pandemic, and associated social restrictions, however, most treatments for schizophrenia-spectrum disorders are offered in-person. Social restrictions associated with COVID-19 have made delivering in-person treatment problematic, and many services have either been delayed or moved to virtual delivery. However, it is unclear what interventions have an evidence-base for virtual delivery.

Objectives: The objectives of the current knowledge synthesis were to:

1) Determine which evidence-based interventions for schizophrenia-spectrum disorders have been empirically examined for virtual delivery
2) For any interventions that have been studied for virtual delivery, determine the efficacy of virtual delivery through meta-analysis

Methods: Ten separate systematic reviews were conducted to examine virtual delivery for each of the ten evidence-based psychological interventions for schizophrenia-spectrum disorders recommended by the American Psychological Association: assertive community treatment, cognitive adaptation training, cognitive behavioural therapy, cognitive remediation, family psychoeducation, illness management and recovery, social learning / token economy, social skills training, supported employment, and acceptance commitment therapy.

Results: Only cognitive remediation, cognitive-behavioural therapy, and family psychoeducation have more than two studies examining their efficacy through virtual care. Virtual delivery of cognitive remediation produced moderate effects on neurocognition ($g = 0.35$) and functioning ($g = 0.33$). Virtual delivery of cognitive behavioural therapy produced moderate effects on symptoms ($g = 0.39$) and small effects on functioning ($g = 0.18$). There were insufficient studies of family psychoeducation with equivalent outcome measures to assess quantitatively, however, studies of virtually delivered family psychoeducation suggested that it is feasible, acceptable, and potentially effective. Delivery through mobile applications was the most common virtual delivery method and few studies compared in-person to remote delivery of the same intervention.

Conclusions: Overall there is a clear lack of evidence for the virtual delivery of evidence-based interventions for schizophrenia. The studies that have been conducted are promising, however, further research is required to determine how to make remote delivery most effective. Of the examined interventions, cognitive remediation has the most evidence for virtual delivery, with effect sizes similar to those observed in meta-analyses of the intervention. Cognitive behavioural therapy and family psychoeducation have also demonstrated some promising studies of virtual delivery, however, future research is required. Examining the virtual delivery of psychological interventions for schizophrenia should be a critical research priority to ensure this population has access to services when in-person services are not possible.

BACKGROUND

Schizophrenia-spectrum Disorders

Schizophrenia-spectrum disorders are the most persistent, debilitating, and economically burdensome mental illnesses worldwide.[1–3] Schizophrenia is associated with a 15-20 year decrease in life expectancy, 5-fold increase in likelihood of death by suicide,[4] and a significant decrease in quality of life.[5] Individuals with severe mental illnesses such as schizophrenia are projected to be among those most affected by the COVID-19 pandemic and to experience deterioration in symptoms and functioning during this time.[6]

Evidence-Based Interventions for Schizophrenia

Despite the persistence and economic impact of schizophrenia-spectrum disorders, psychosocial interventions have demonstrated significant ability to improve quality of life,[7] decrease hospitalizations,[8] and reduce economic impact.[9] Psychosocial interventions are widely recommended in clinical guidelines for the treatment of schizophrenia-spectrum disorders in Canada[10] and internationally.[11] In fact, the American Psychological Association has recommended that ten different psychosocial interventions are evidence-based for the treatment of schizophrenia-spectrum disorders: Assertive Community Treatment, Cognitive Adaptation Training, Cognitive Behavioural Therapy, Cognitive Remediation, Family Psychoeducation, Illness Management and Recovery, Social Learning / Token Economy Programs, Social Skills Training, Supported Employment, and Acceptance and Commitment Therapy.[12] Social restrictions as a result of the COVID-19 pandemic have limited the availability of these interventions delivered through traditional, in-person, methods. In order to maintain access to care during the pandemic, services across the country have gravitated towards telehealth and internet-based delivery methods. However, it is unlikely that all interventions that are evidence-based for in-person delivery are also evidence-based for virtual delivery. During the COVID-19 pandemic individuals with schizophrenia-spectrum disorders are experiencing a lack of access to in-person services due to social restrictions and the efficacy of virtual care for this population is unclear.[13] Some have suggested that internet-based interventions may actually cause harm.[14] Given the exclusive delivery of virtual services in most Canadian mental health programs during the COVID-19 pandemic it is critical to determine whether virtual service delivery is effective. This is the first systematic review to examine the evidence-base for delivering in-person evidence-based interventions for schizophrenia through virtual care.

Objectives

1) Determine which evidence-based interventions for schizophrenia-spectrum disorders have been empirically examined for virtual delivery
2) For any interventions that have been studied for virtual delivery, determine the efficacy of virtual delivery through meta-analysis

METHODS

Ten separate systematic reviews were conducted to examine each of the ten distinct evidence-based treatments recommended by the American Psychological Association for the treatment of schizophrenia-spectrum disorders (Table 1).

Eligibility Criteria

To be included in the review studies had to meet the following criteria: 1) participants were diagnosed with a majority (> 50%) schizophrenia-spectrum disorders, 2) the experimental treatment was the specific treatment in question, 3) the treatment must be delivered by some form of remote method that was not in-person, 4) any control condition or non-controlled study was acceptable, 5) were published in peer-reviewed journals, and 6) no conference abstracts or clinical trial registrations, only full papers were selected.

Table 1: Evidence-Based Interventions for Schizophrenia-Spectrum Disorders

1	Assertive Community Treatment
2	Cognitive Adaptation Training
3	Cognitive Behavioural Therapy
4	Cognitive Remediation
5	Family Psychoeducation
6	Illness Management and Recovery
7	Social Learning / Token Economy Programs
8	Social Skills Training
9	Supported Employment
10	Acceptance and Commitment Therapy

Information Sources

Literature searches were conducted following PRISMA guidelines using three databases: Ovid MEDLINE, EMBASE, and PsycINFO from January 1990 to May 2020 in order to encompass all possible approaches to delivering interventions through remote-delivery methods. The Cochrane central registry of controlled trials was also searched to determine whether any clinical trials were registered that may have been missed in the database search. The reference lists of relevant papers and relevant reviews were also searched to identify any relevant papers that were missed in the initial search. Searches were restricted to papers published in English.

Search Strategy

Within each database ten different searches were conducted – one for each intervention approach. Keywords for the intervention-specific search terms were developed by examining the search strategies of relevant systematic reviews of the target intervention. The following search strategy was used for each search:

1) The sample consisted of a majority of participants with schizophrenia-spectrum disorders

   Search Terms: “psychotic” OR “psychosis” OR “schizo*”

2) The treatment approach was delivered through virtual care

   Search Terms: “computer” OR “phone” OR “tablet” OR “mobile” OR “internet” OR “online” OR “web” OR “app” OR “virtual” OR “telehealth” OR “remote”

3) Separate searches for the specific intervention used

   <u>Assertive Community Treatment</u>
   Search Terms: “assertive community treatment” OR “case management”

   <u>Cognitive Adaptation Training</u>
   Search Terms: “cognitive adaptation training” OR “CAT”

Cognitive Behavioural Therapy
Search Terms: "cognitive therap*" OR "cognitive behavio?r*" OR "cbt"

Cognitive Remediation
Search Terms: "cognit*" AND ("training" OR "remediation" OR "rehabilitation" OR "enhancement")

Family Psychoeducation
Search Terms: ("family" OR "carer" OR "caregiver" OR "relative" OR "spouse" OR "partner") AND ("psychoeducation" OR "intervention" OR "treatment" OR "program")

Illness Management and Recovery
Search Terms: "illness management and recovery" OR "wellness management and recovery" OR "IMR"

Social Learning / Token Economy Programs
Search Terms: "token economy" OR "behavio?r therapy" OR "social learning" OR "operant conditioning"

Social Skills Training
Search Terms: "social skills training" OR "social training" OR "skills training"

Supported Employment
Search Terms: "supported employment" OR "individual placement and support"

Acceptance and Commitment Therapy
Search Terms: "acceptance and commitment therapy" OR "ACT"

Study Selection

The results of all searches were imported into Covidence systematic review software for further selection. All titles and abstracts were initially reviewed by two raters for relevance and any conflicts between ratings were resolved by the PI (MWB). Following title and abstract screening, full-texts were reviewed by two raters and conflicts were again resolved by MWB. Data extraction was then conducted for all studies that met inclusion criteria. Data on relevant outcome measures were extracted including symptoms, functioning, and quality of life.

Meta-Analyses

Due to the small number of studies that met inclusion criteria, a fixed effects meta-analysis was conducted. Random-effects models are imprecise at small sample sizes. All meta-analyses were conducted using R, and pooled effect sizes were calculated using Hedges *g*, which corrects for overestimation in small sample studies.

RESULTS

PRISMA search diagrams for each search are presented in Appendix A. A list of all studies that met inclusion criteria is included in Appendix B.

Assertive Community Treatment

No studies met inclusion criteria for an Assertive Community Treatment program delivered remotely. Two interventions were developed to support case managers in implementing cognitive-behavioural approaches to case management, however, these are discussed in the Cognitive-Behavioural Therapy Review as this was targeted at a specific intervention rather than at a broader approach to implementing Assertive Community Treatment through virtual care.

Cognitive Adaptation Training

Cognitive Adaptation Training has only been examined through in-person interventions. No studies met criteria for remote delivery.

Cognitive Behavioural Therapy

Eight studies examined various forms of cognitive-behavioural interventions, however, only four studies reported outcome data. All four studies reported results for total symptoms and three out of the four studies reported results for functioning. Two studies used the Positive and Negative Syndrome Scale to assess symptoms and two studies used the Brief Psychiatric Rating Scale. All studies used different functioning measures. One study used the Personal and Social Performance scale, one used the Specific Levels of Functioning, and one used the First-Episode Social Functioning Scale. Only two studies included a control condition.[15,16]

Bucci et al. (2018) conducted a proof-of-concept study of an app called Actissist. Actissist invites participants to access the app at regular intervals and the app contains a range of content including videos, and cognitive behavioural therapy tools. The app helps participants track their symptoms and experiences, and prompts participants to reappraise their initial appraisals of situations. Compared to a comparison app, Actissist produced larger improvements in symptoms and functioning.

Another app called CBT2GO[16] uses algorithms to display interactive content tailored to the cognitions that participants endorse. For example, participants are asked about a symptom, if they endorse the symptom then they are given a list of possible dysfunctional beliefs they might hold about the symptom, and then the app provides suggestions of possible more adaptive beliefs that could replace the dysfunctional belief. Compared to a comparison mental health app, CBT2GO produce larger improvements in functioning and cognitions.

Lastly, the HORYZONS online system is a moderated and interactive online therapy system unlike the apps discussed thus far. The HORYZONS program integrates peer-

Table 2: Fixed effects meta-analysis of cognitive behavioural therapy without consideration of a control group on symptoms

Study	g(s.e.)	Z	p
Bucci et al. 2018	0.840(0.153)	5.505	4e-08
Depp et al. 2019	0.357(0.068)	5.240	2e-07
Alvarez-Jimenez et al. 2013	0.037(0.118)	0.318	0.751
Ludwig et al. 2020	0.778(0.163)	4.774	2e-06
Summary	0.394(0.052)	7.557	4e-14

to-peer online social networking, individually tailored interventions, and moderation by therapy experts. The program incorporates therapeutic techniques including cognitive restructuring and identification of early warning signs of relapse. In the initial trial, HORYZONS was acceptable and significantly improved depression symptoms.[17] A follow-up study found similarly promising results on acceptability and symptoms.[18]

Other programs and apps have also been developed but have been evaluated less extensively. The MATS app consists of computer-initiated text message to a smartphone application to prompt individuals to rate domains relating to experiencing hallucinations, medication adherence, and social activities.[19] Participants are prompted three times daily with these questions and based on responses cognitive-behavioural interventions are implemented through text message. The Heal Your Mind app was developed to facilitate cognitive-behavioural case management and demonstrated initial acceptability to clients.[20] An online moderated social anxiety treatment (EMBRACE) demonstrated efficacy to improve social anxiety symptoms, however, other symptoms and functioning were not examined.[21]

Table 3: Fixed effects meta-analysis of cognitive behavioural therapy without consideration of a control group on functioning

Study	g(s.e.)	Z	p
Bucci et al. 2018	0.387(0.163)	2.376	0.017
Depp et al. 2019	0.143(0.102)	1.411	0.158
Ludwig et al. 2020	0.048(0.165)	0.291	0.771
Summary	0.176(0.076)	2.310	0.021

Table 4: Fixed effects meta-analysis of cognitive behavioural therapy compared to a control group on symptoms

Study	g(s.e.)	Z	p
Bucci et al. 2018	0.760(0.193)	3.949	8e-05
Depp et al. 2019	0.047(0.091)	0.516	0.606
Summary	0.177(0.082)	2.154	0.031

Table 5: Fixed effects meta-analysis of cognitive behavioural therapy compared to a control group on functioning

Study	g(s.e.)	Z	p
Bucci et al. 2018	0.630(0.287)	2.195	0.028
Depp et al. 2019	0.182(0.149)	1.219	0.223
Summary	0.277(0.132)	2.093	0.036

Meta-Analysis

Meta-analyses were conducted separately for outcomes on symptoms and functioning. We also calculated separate meta-analytic estimates for raw change scores from pre- to post- treatment and compared to change in control groups.

When examining change from pre- to post- treatment among all four included studies, a moderate effect size ($g = 0.39$) was found for symptoms and a small effect size was found for functioning ($g = 0.18$; Tables 2 & 3). When the two studies including a control group were examined and effect sizes were calculated relative to the control group, the effect size on symptoms was $g = 0.18$ (Table 4) and on functioning was $g = 0.28$ (Table 5).

Cognitive Remediation

Seven studies met inclusion criteria for virtually delivered cognitive remediation (CR). Three of these studies used the Posit Science Brain HQ platform,[22–24] two studies used a form of working

memory training,[25,26] one study used COGWEB,[27] and one study used a combination of cognitive training programs.[28] This represents a variety of approaches to CR including "bottom-up training" (Posit Science) and "top-down training" (working memory training). The primary outcome measures in these studies were neurocognitive abilities and community functioning. All studies except one[28] assessed neurocognition as an outcome. The MATRICS Consensus Cognitive Battery was the most commonly used measure (n = 3), followed by the Weschler Abbreviated Scale of Intelligence (n = 2) and Wisconsin Card Sorting Test (n = 1). All but one study[26] also assessed functioning. The most commonly used measure was the Strauss-Carpenter Scale (n = 2), followed by the Social Functioning Scale (n = 1), Social and Occupational Functional Assessment Scale (n = 1), Role Functioning Scale (n = 1), and the Personal and Social Performance Scale (n = 1). Two studies did not include a control condition[24,27] and the others included a variety of control conditions ranging from treatment as usual to active control conditions. Additionally, only one study included a follow-up assessment.[25] One study[22] compared at-home iPad-based cognitive remediation to cognitive remediation delivered in the laboratory on desktop computers. This was not a randomized controlled trial, but instead resulted from a transition in delivery method part-way through a larger clinical trial. This was the only study that directly compared at-home cognitive remediation with in-person cognitive remediation and it found that there were no differences in engagement, cognition, functioning, or quality of life between the two delivery methods. Thus, this preliminary study would suggest that at-home delivery of cognitive remediation may be feasible and produce equivalent effects to in-person delivery.

Table 6: Fixed effects meta-analysis of cognitive remediation without consideration of a control group on neurocognition

Study	g(s.e.)	Z	p
Biagianti et al. 2017	-0.001(0.093)	-0.007	0.995
Donohoe et al. 2018	0.588(0.087)	6.727	2e-11
Fisher et al. 2015	0.538(0.094)	5.753	9e-09
Hargreaves et al. 2015	0.179(0.096)	1.868	0.062
Melo Moura et al. 2019	0.358(0.246)	1.452	0.146
Ventura et al. 2013	0.483(0.196)	2.469	0.014
Summary	0.345(0.044)	7.797	6e-15

Table 7: Fixed effects meta-analysis of cognitive remediation without consideration of a control group on functioning

Study	g(s.e.)	Z	p
Biagianti et al. 2017	0.129(0.143)	0.896	0.370
Donohoe et al. 2018	0.951(0.140)	6.810	1e-11
Fisher et al. 2015	0.126(0.107)	1.179	0.238
Harris et al. 2017	0.079(0.145)	0.544	0.586
Melo Moura et al. 2019	0.699(0.252)	2.771	0.006
Ventura et al. 2013	0.502(0.255)	1.968	0.049
Summary	0.332(0.061)	5.423	6e-08

Table 8: Fixed effects meta-analysis of cognitive remediation compared to a control group on neurocognition

Study	g(s.e.)	Z	p
Biagianti et al. 2017	-0.306(0.148)	-2.061	0.038
Donohoe et al. 2018	0.508(0.106)	4.795	2e-06
Fisher et al. 2015	0.426(0.111)	3.836	1e-04
Hargreaves et al. 2015	0.168(0.132)	1.275	0.202
Summary(all)	0.276(0.060)	4.571	5e-06
Summary(exclude B2017)	0.393(0.066)	5.927	3e-09

Meta-Analysis

Meta-analyses were conducted separately for outcomes on neurocognition and functioning. We also calculated separate meta-analytic estimates for raw change scores from pre- to post- treatment and compared to change in control groups. Effect sizes on neurocognition (g = 0.34) and functioning (g = 0.33) were moderate Tables 6 & 7.

Among the five studies that included a control group, four studies had inactive controls while one study had an active control condition.[22] Effect sizes were calculated for all five studies compared to the control group, and then were also calculated excluding the study by Biagianti et al. (2017) to determine whether the effect size changed substantially without the active control condition. When Biagianti et al. (2017) was included, the effect size on neurocognition was g = 0.28, however, when Biagianti et al. (2017) was excluded the effect size was g = 0.39 (Table 8). When Biagianti et al. (2017) was included the effect size on functioning was g = 0.15, however, when Biagianti et al. (2017) was excluded the effect size was g = 0.22 (Table 9).

Table 9: Fixed effects meta-analysis of cognitive remediation compared to a control group on functioning

Study	g(s.e.)	Z	p
Biagianti et al. 2017	-0.172(0.222)	-0.775	0.438
Donohoe et al. 2018	0.544(0.161)	3.379	0.001
Fisher et al. 2015	-0.097(0.153)	-0.632	0.527
Harris et al. 2017	0.272(0.232)	1.171	0.241
Summary(all)	0.153(0.091)	1.680	0.093
Summary(exclude B2017)	0.220(0.100)	2.193	0.028

Family Psychoeducation

Seven studies examined family psychoeducation programs delivered through virtual delivery options. Most studies did not include long-term follow-up, however, one study included follow-up one year later. Additionally, there were few consistent measures used across studies, which made estimating effect sizes through meta-analysis infeasible. Some studies examined outcomes on individuals with schizophrenia, whereas other studies assessed outcomes on the family members.

Two papers related to a single study of internet-based psychoeducational interventions for people with schizophrenia and their family members.[29,30] In this study a website was developed that included online therapy groups for family members, or people with schizophrenia, or combined therapy for both the family member and the service-user. There was a section of the website to ask questions, a library of previously asked questions, and educational resources to learn more about schizophrenia. The website and groups were accessed frequently up to three months after the website launched[29] and one year after using the website positive symptoms had decreased for the participants with schizophrenia and they had increased knowledge about schizophrenia.

One proof-of-concept study examined an online support program for relatives of people with schizophrenia, which consisted of a discussion board, links to other agency resources, written information, brief educational video clips, and a real-time chat.[31] This program demonstrated feasibility and participants were generally satisfied with the online experience. Other studies found that telepsychiatry may be equivalent to in-person for delivering family psychoeducation[32] and that online family psychoeducation can improve symptoms for individuals with schizophrenia.[33] Lastly, a case study provided initial evidence that using a web camera for family-focused interventions is possible in forensic settings in which it may not be possible for family members to attend in person.[34]

Generally, studies on virtual delivery of family psychoeducation focused on feasibility and satisfaction measures, and few focused on outcomes. Those that did focus on outcomes suggested that

family psychoeducation delivered through virtual methods improves family knowledge and service-user well-being, however, the evidence is very preliminary.

Illness Management and Recovery

Two studies examining one Illness Management and Recovery program met inclusion criteria for virtual delivery. Both studies examined the FOCUS app, which includes three components: the FOCUS app, clinician dashboard, and mental health support specialist.[35,36] The FOCUS app uses self-assessment prompts targeting self-management content in five domains: coping with voices, mood, sleep hygiene, social functioning, and medication. Content consists of audio clips, video clips, and written material. FOCUS participants also received brief weekly phone calls from a mental health support specialist to assist with both technical and clinical support.

FOCUS was compared to an in-person program with similar features called Wellness Recovery Action Plan (WRAP) in a randomized controlled trial. Although not powered for non-inferiority, FOCUS demonstrated similar improvements in symptoms, quality of life and recovery to the in-person WRAP treatment. More participants also initiated treatment after randomization in the FOCUS group (90%) than in the WRAP group (58%). This difference remained halfway through treatment, however, disappeared by the end of treatment. A subsequent qualitative analysis of FOCUS[36] found three main themes that participants highlighted as valuable about the FOCUS intervention. First, the app served as support that could be accessed at any time and anywhere, making it especially helpful during periods when a participant may not be able to contact their case manager or psychiatrist. Second, the app helped participants feel in control of their symptoms due to the immediate feedback of strategies for whatever they might currently be experiencing. Lastly, participants indicated that FOCUS facilitated their own self-awareness about their experiences and made them more aware of when they might need additional supports to cope.

Social Learning / Token Economy Programs

One study met criteria for delivering a social learning or behavioural intervention through remote delivery. This study examined the development of an app for smoking cessation in schizophrenia called the Multi-Component Mobile-enhanced Treatment for Smoking Cessation (iCOMMIT).[37] In the iCOMMIT app participants receive monetary compensation on a daily basis according to their levels of CO. Using a smartphone, participants could blow into a small CO monitor and if they met criteria for abstinence then they would receive compensation. This study reports a preliminary cohort of 5 participants who received this intervention with 2 of the 5 participants demonstrating significant decreases in smoking behaviour. In a second cohort, pharmacotherapy was added and 3 out of 8 participants reported abstinence at the end of treatment. Although, this was a small preliminary study, it appears that contingency management may be feasible for smoking cessation through a virtual app.

Social Skills Training

Social skills training has only been examined in-person. No studies met our inclusion criteria for social skills training delivered through virtual care.

Supported Employment

Supported employment has only been examined in-person. No studies met our inclusion criteria for supported employment.

Acceptance and Commitment Therapy

Of the relevant papers examining Acceptance and Commitment Therapy, only 1 study met the inclusion criteria for delivery of the treatment through a virtual delivery method. This study examined the Learn to Quit smoking cessation app, which utilizes principles of Acceptance and Commitment Therapy to specifically reduce smoking among individuals with schizophrenia-spectrum disorders.[38] This was a small case-series of 7 participants comparing the Learn to Quit app to a control app developed for the general population. There was suggestion that five out of the seven participants experienced reductions in smoking, however, it is unclear how long these reductions were maintained, or whether these could be considered clinically significant reductions in smoking behaviour.

DISCUSSION

The present synthesis highlights the general lack of empirical research that has been conducted to date on virtual delivery of evidence-based interventions for schizophrenia. Most of the research that has been conducted has been done in the past 5 – 10 years and it appears that it is only select research groups who have undertaken attempts to develop effective remote delivery options for schizophrenia. Decades of research have gone into developing evidence-based interventions for the in-person treatment of schizophrenia however, it is largely unclear to what extent this evidence-base will transfer to virtual delivery of these interventions. Although the COVID-19 pandemic has created a situation in which we are forced to either postpone psychological treatment or deliver it virtually, we have an extremely limited evidence-base to make these decisions. It would seem in the current pandemic that delivery of evidence-based interventions through virtual care is advisable, however, long-term it is important to consider whether interventions are equally effective virtually.

Four of the ten examined interventions had no published studies examining virtual delivery (assertive community treatment, cognitive adaptation training, social skills training, and supported employment). An additional two interventions (acceptance and commitment therapy, and social learning / token economy programs) only had one study examining virtual delivery and both were focused on smoking cessation. Illness management and recovery had been examined in two papers however, both examined the same mobile app and only one provided quantitative data. Thus, only three of the examined interventions (cognitive behavioural therapy, cognitive remediation, and family psychoeducation) had a sufficient number of studies to consider qualitative and quantitative syntheses. The outcomes from family psychoeducation were too disparate to synthesize quantitatively, thus meta-analyses were only conducted for cognitive behavioural therapy and cognitive remediation.

App-based delivery of the examined interventions was the most common format, and only two programs (cognitive behavioural therapy[17,18] and family psychoeducation[29,39] examined delivery of the interventions through a form of virtual therapist contact (e.g. teletherapy or online therapy). Most studies found app-based delivery methods to be acceptable and feasible to participants, thus, app-based interventions may be a feasible form of low-intensity treatment.

Implications for Clinical Care

Given the limited evidence available for psychological interventions delivered through virtual care, it is important to consider that there is currently insufficient evidence to fully recommend any intervention through virtual delivery methods. Of the three interventions that have a sufficient number of studies examining virtual delivery, both cognitive remediation and cognitive behavioural therapy demonstrated reasonable effect sizes. Cognitive remediation moderately improved neurocognition (g = 0.35) and functioning (g = 0.33), which are just slightly lower than meta-analytic estimates of cognitive remediation effects on neurocognition (g = 0.45) and functioning (g = 0.37).[40] Thus, cognitive remediation may be able to produce similar results when delivered remotely to when it is delivered in person. When cognitive behavioural therapy was delivered remotely, effects on symptoms (g = 0.39) and functioning (g = 0.17) were also similar to effect sizes found in meta-analyses.[41,42] Cognitive-behavioural therapy had substantially fewer studies examining virtual delivery, thus, these results should be interpreted cautiously. Finally, family psychoeducation appears to be feasible and acceptable for remote delivery, however, more systematic measurement across studies is necessary to examine this quantitatively.

The format of virtual delivery should also be considered. Cognitive remediation and family psychoeducation were able to be delivered with limited changes in the virtual environment. For example, cognitive remediation interventions still emphasized computerized practice of cognitive training exercises like they do in-person, and family psychoeducation still emphasized providing information to the family about schizophrenia. The main change was that this was done without the individual or family needing to come into sessions in-person. Delivery of the cognitive-behavioural therapy interventions could be considered to be a dramatic departure from typical cognitive-behavioural therapy which often involves components of going into the community and conducting behavioural experiments to test out dysfunctional appraisals. The interventions that have delivered cognitive-behavioural interventions virtually have focused on implementing specific cognitive-behavioural tools (such as thought records) or on generating pre-specified algorithms to help evaluate appraisals. These are likely to be lower intensity interventions, thus it is unclear what patient characteristics may predict who responds to these approaches and who may require full cognitive behavioural therapy. It will be important to examine full individualized cognitive-behavioural therapy delivered through virtual care, in addition to these application-based programs.

The ability of clinicians to deliver some of the examined evidence-based interventions through virtual care may also be challenging. For example, cognitive adaptation training and assertive community treatment by definition involve going to an individual's home and working with them in their home environment. Although this may be possible through virtual care, it will present additional challenges to virtually navigate the home environment that other therapeutic modalities may not. Similarly, supported employment involves participants being supported in a physical workplace. Although, this may be possible to do in virtual work environments, many supported employment settings involve physical work and it is unclear how feasible virtual supported employment might be.

Additional clinical consideration may also need to be given to the delivery of symptom-focused therapies for virtual delivery. For example, cognitive-behavioural therapy and acceptance and commitment therapy could be delivered through virtual meetings like teletherapy or video therapy, however, consideration is likely needed regarding the type of experiences that are explored in this setting. For example, traumatic experiences may not be appropriate to explore over a virtual platform, however, without evidence examining this it is challenging to make concrete recommendations for treatment delivery.

Implications for Research

It is clear that there is an urgent need for research to validate psychological interventions for schizophrenia-spectrum disorders delivered through virtual delivery. The majority of treatment for schizophrenia is conducted in-person and the current review highlights the paucity, and in many cases absence, of research examining virtual delivery of evidence-based interventions. Pilot studies are likely the fastest way to begin to accumulate this evidence-base in a shorter time-frame, however, it is ultimately going to be necessary to conduct definitive trials, powered for non-inferiority, to determine whether virtual delivery is equally effective to in-person delivery.

Research priorities could be considered in two domains: 1) establishing whether interventions are effective through virtual care; and 2) examining how to optimize interventions for virtual care. Most of the examined interventions currently fall into the first category since there has been an absence of research into the effectiveness of virtual delivery. For family psychoeducation, cognitive remediation, and cognitive-behavioural therapy an appropriate research focus may be better characterized by examining how to optimize and implement the interventions through virtual care. Given the nature of social restrictions during the COVID-19 pandemic, it is likely that there will be similar social restrictions put in place during future crises, and there is an urgent need to develop an evidence-base to inform treatment delivery for people with schizophrenia during such periods.

In addition to developing a quantitative evidence-base it will also be important to consider the experience of service-providers and service-users in virtual interventions. In the reviewed literature, qualitative studies suggested that participants found virtual delivery options to be acceptable, however, it may also be useful to involve service-users in the development of virtual adaptations of interventions to maximize acceptability. Additionally, service-providers must be willing to provide the interventions through virtual care, thus examining the experience of service providers with the interventions will also be important.

CONCLUSION

To date there has been insufficient research examining evidence-based interventions for schizophrenia-spectrum disorders delivered through virtual care. Only cognitive remediation, cognitive-behavioural therapy, and family psychoeducation have more than two studies examining virtual delivery. Preliminary studies suggest that virtual delivery options are feasible and acceptable, thus there is urgent need for larger clinical trials to evaluate the efficacy of these interventions through virtual care. If clinics are uncertain regarding interventions that are most likely to be effective through virtual care, cognitive remediation, cognitive-behavioural therapy, and family psychoeducation are all reasonable candidates based on current evidence, however, further research on how to engage service-users in these interventions and how to implement them on a larger scale is required.

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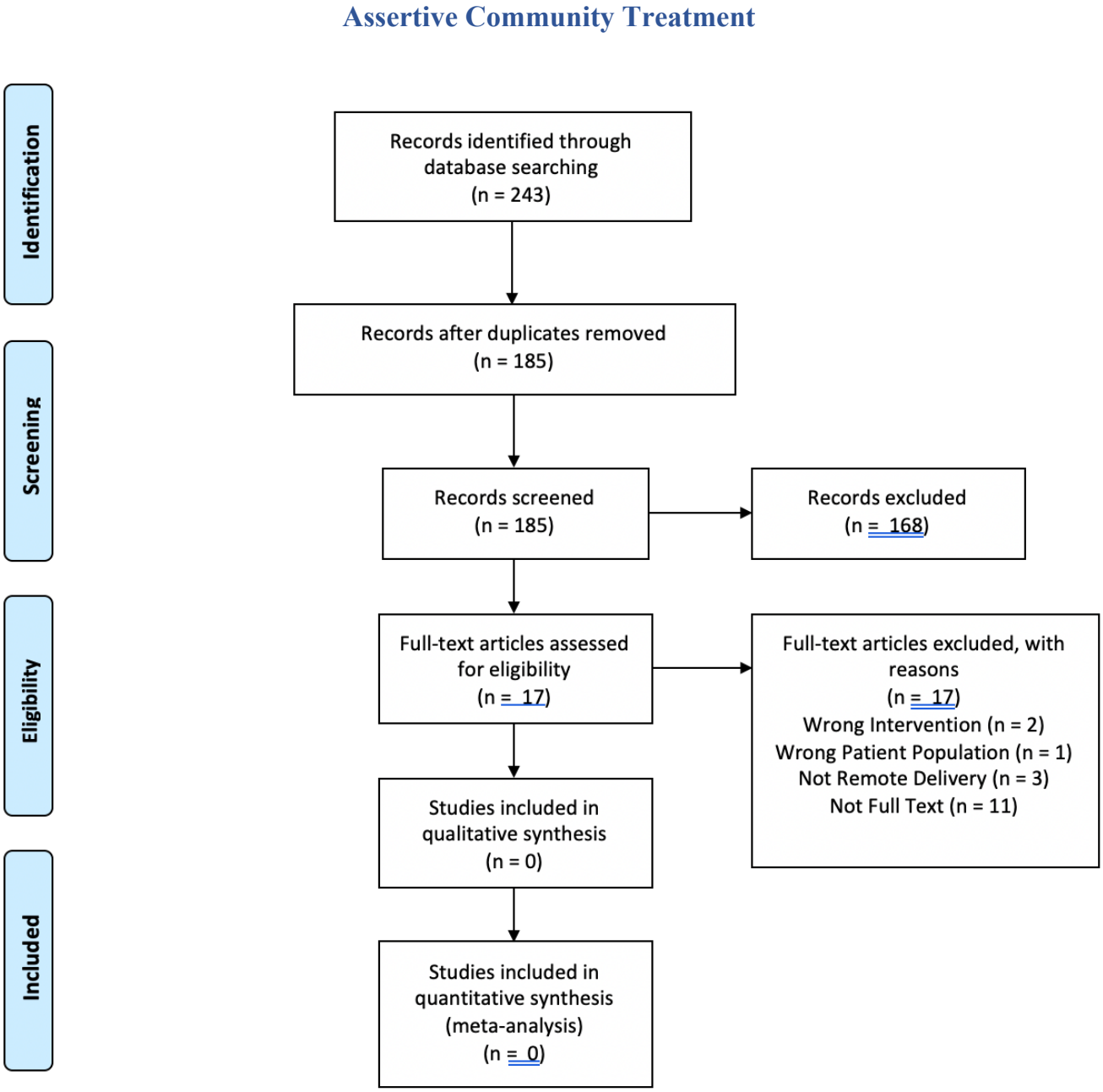
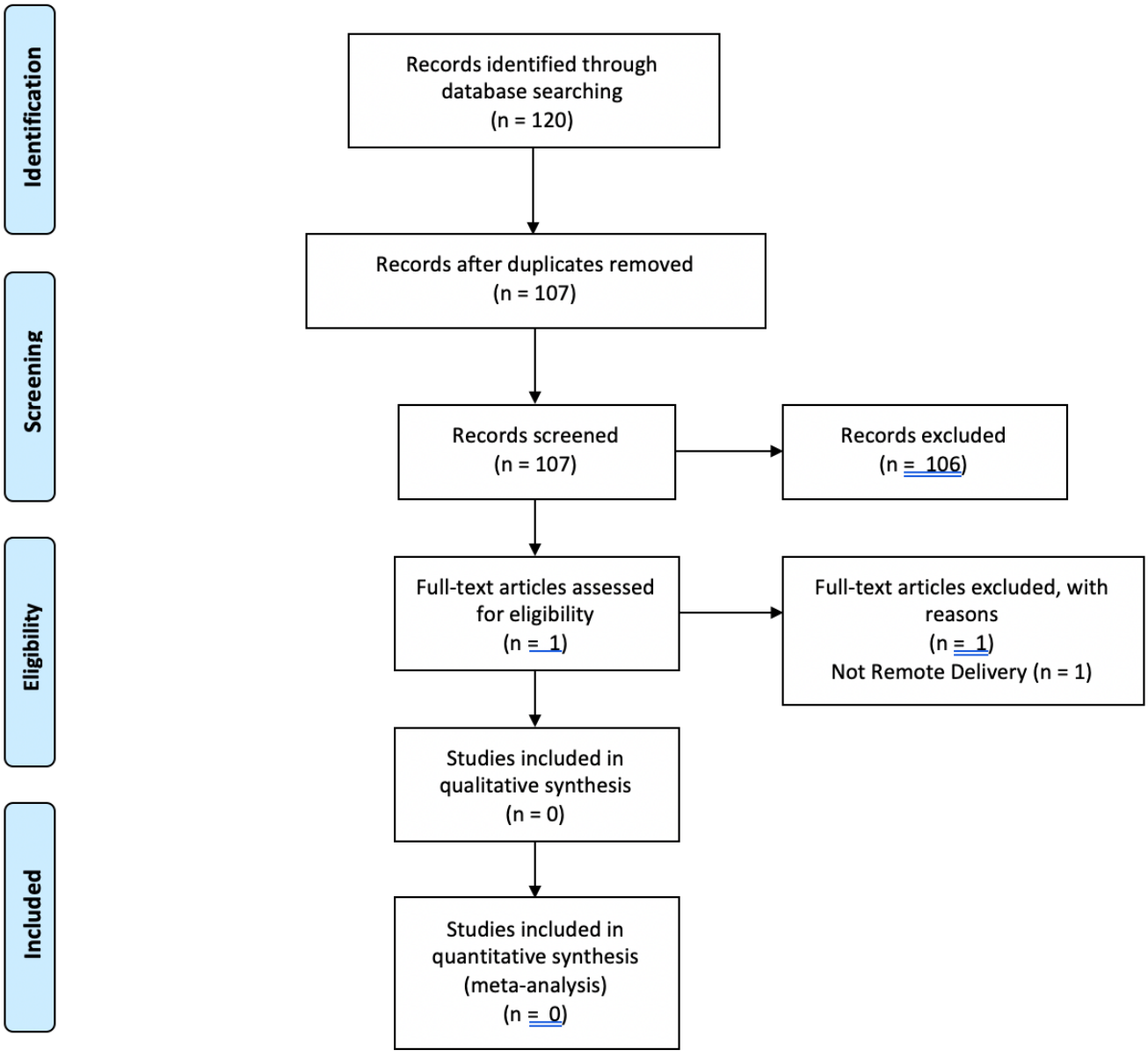
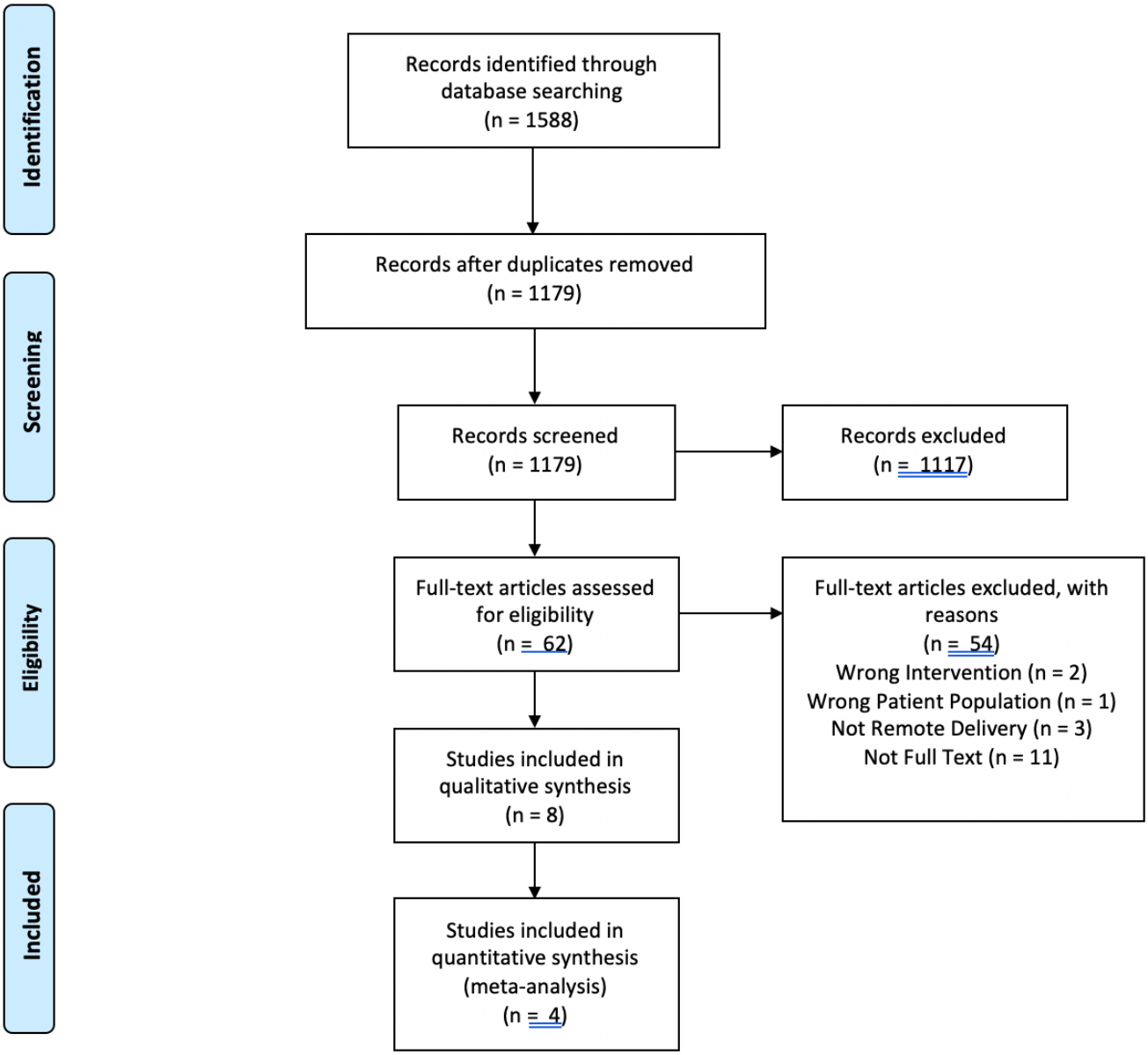
APPENDIX A: PRISMA Diagrams for Systematic Reviews



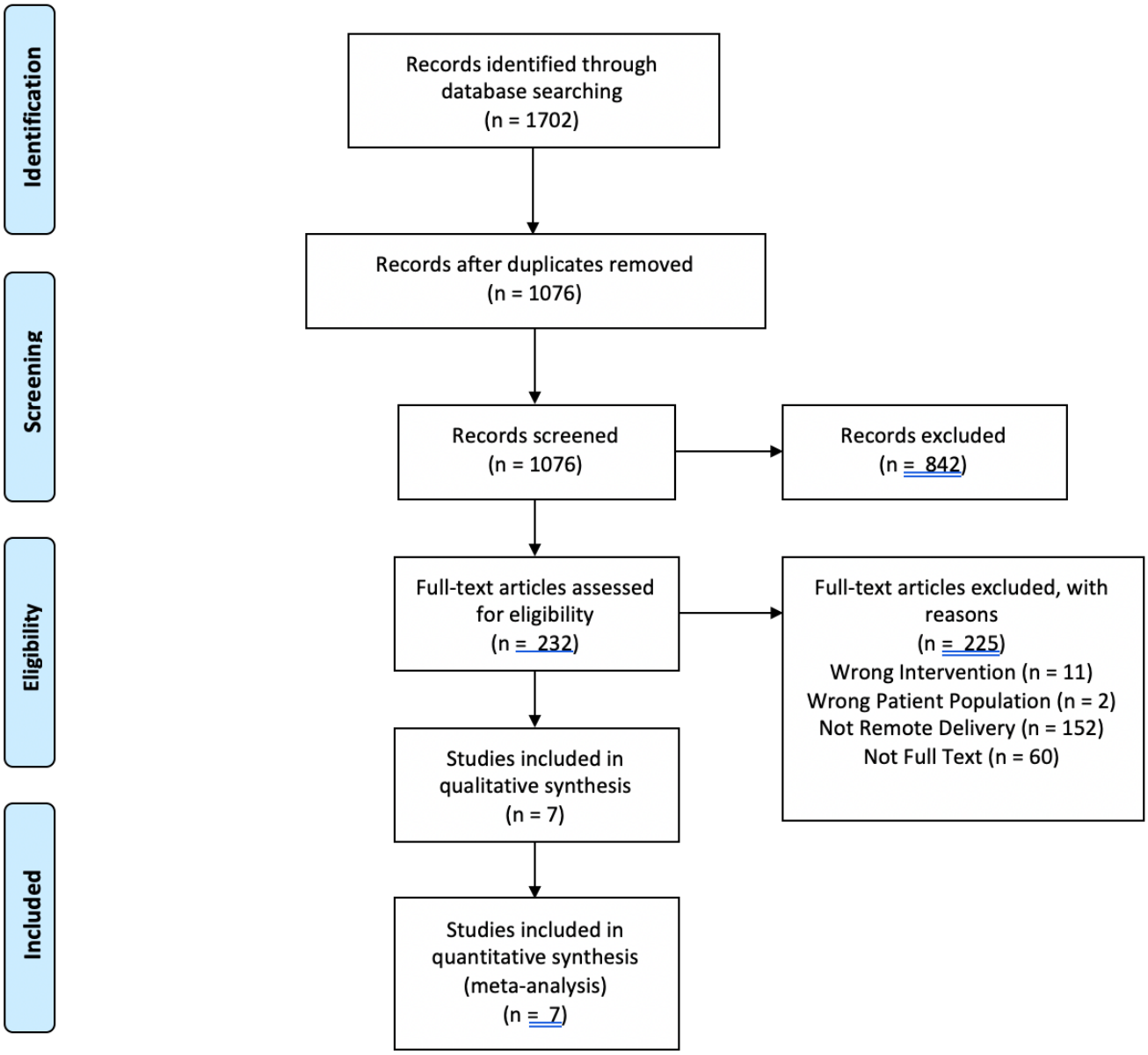
Cognitive Adaptation Training



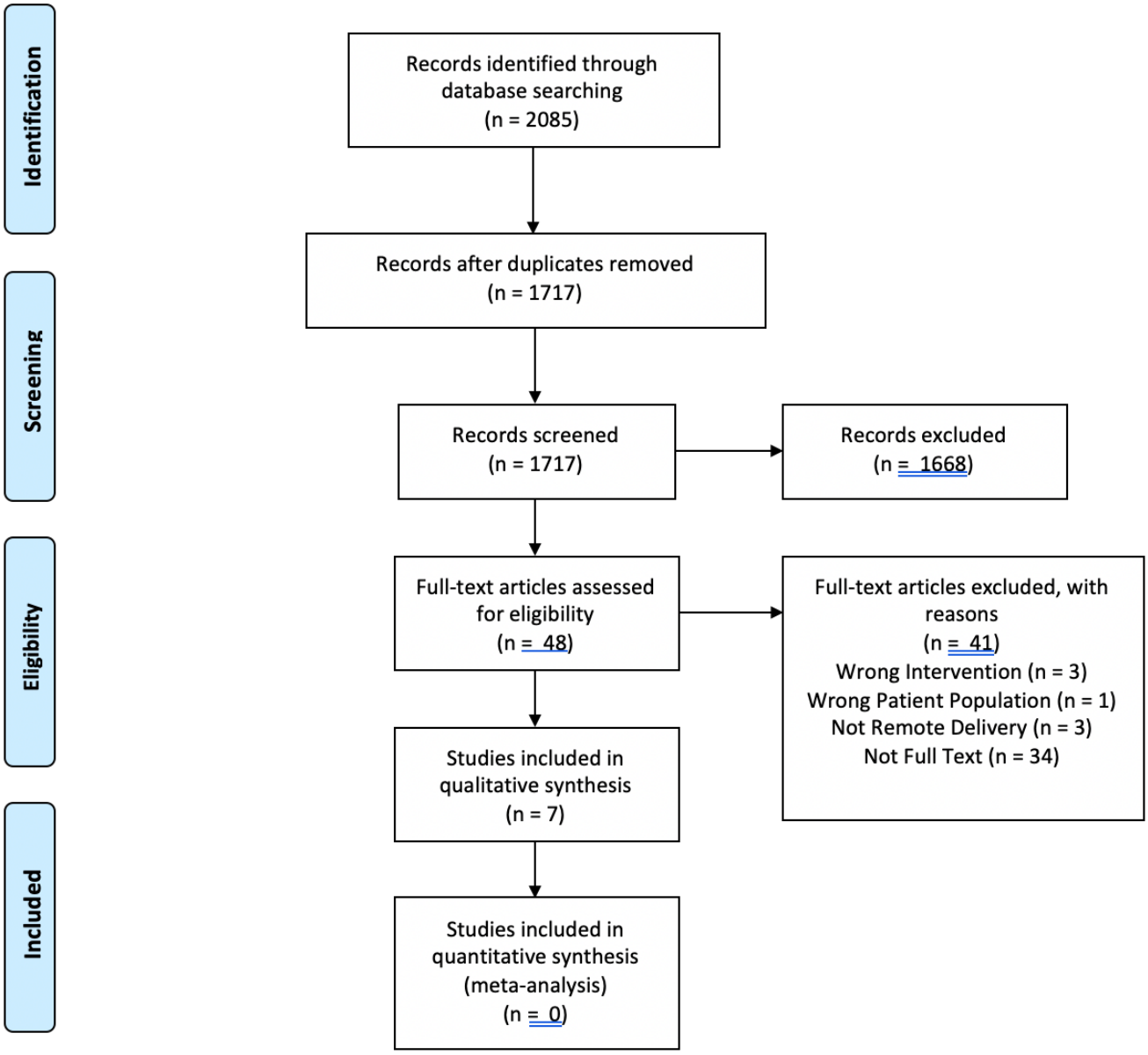
Cognitive Behavioural Therapy



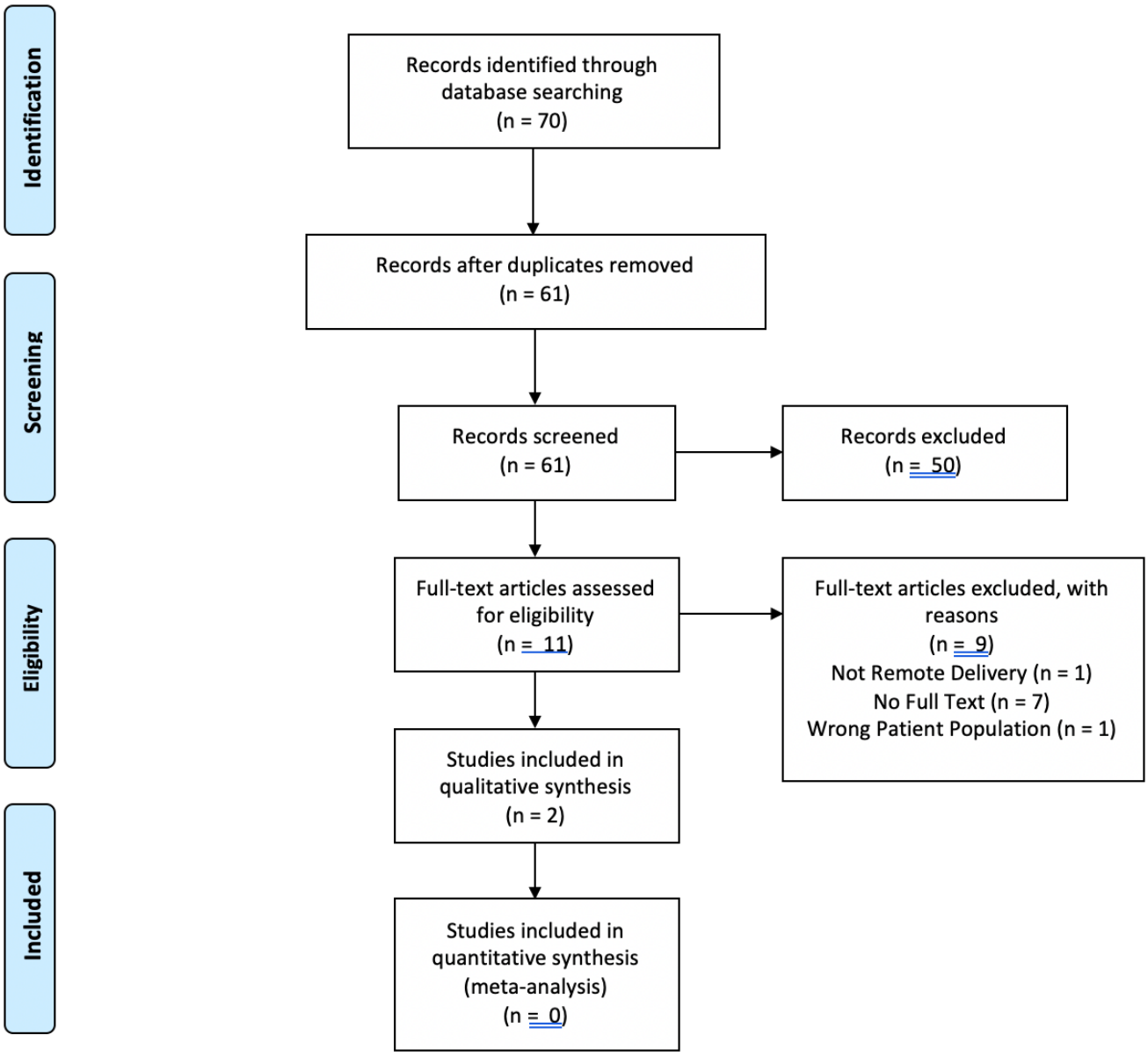
Cognitive Remediation



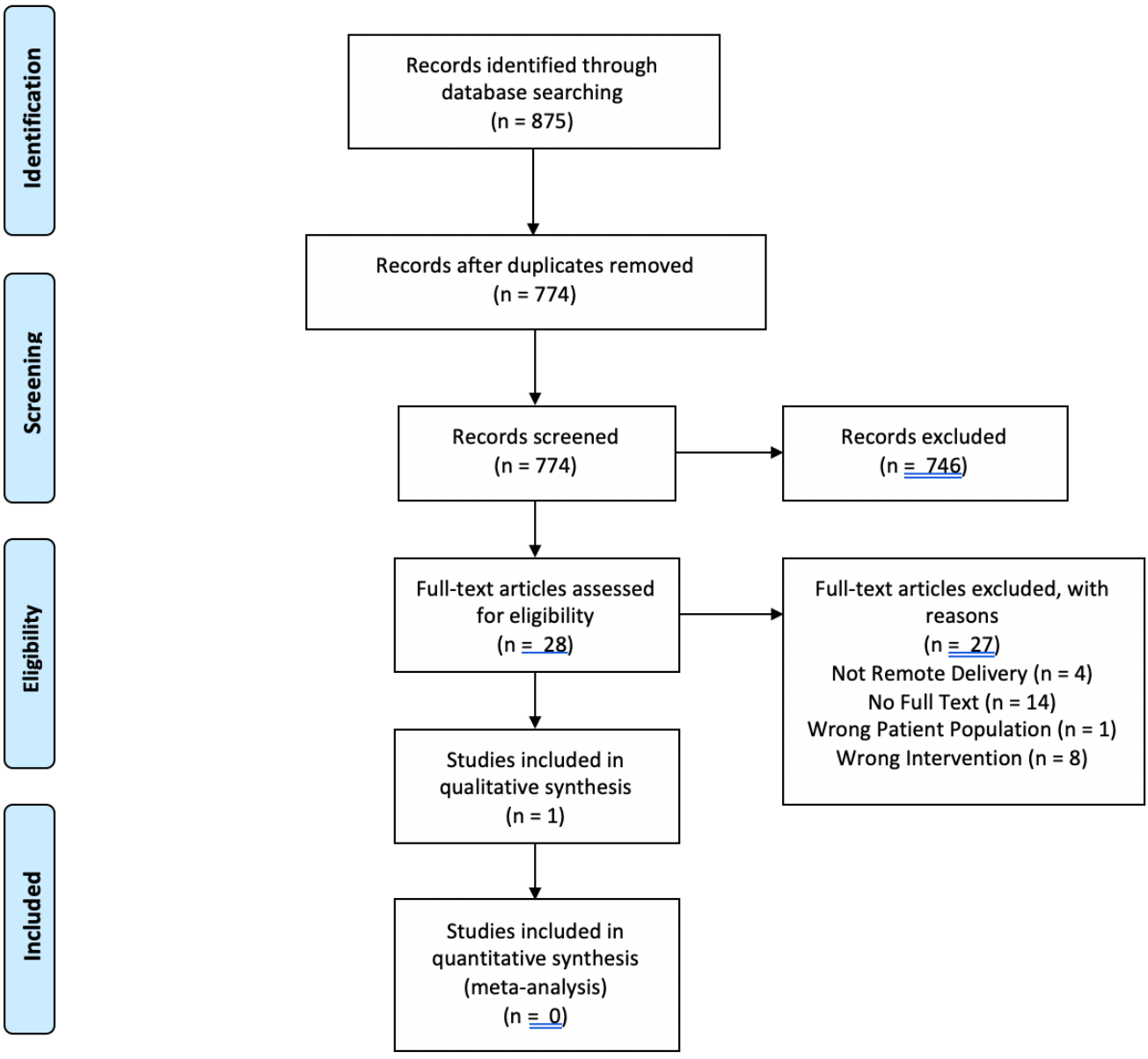
Family Psychoeducation



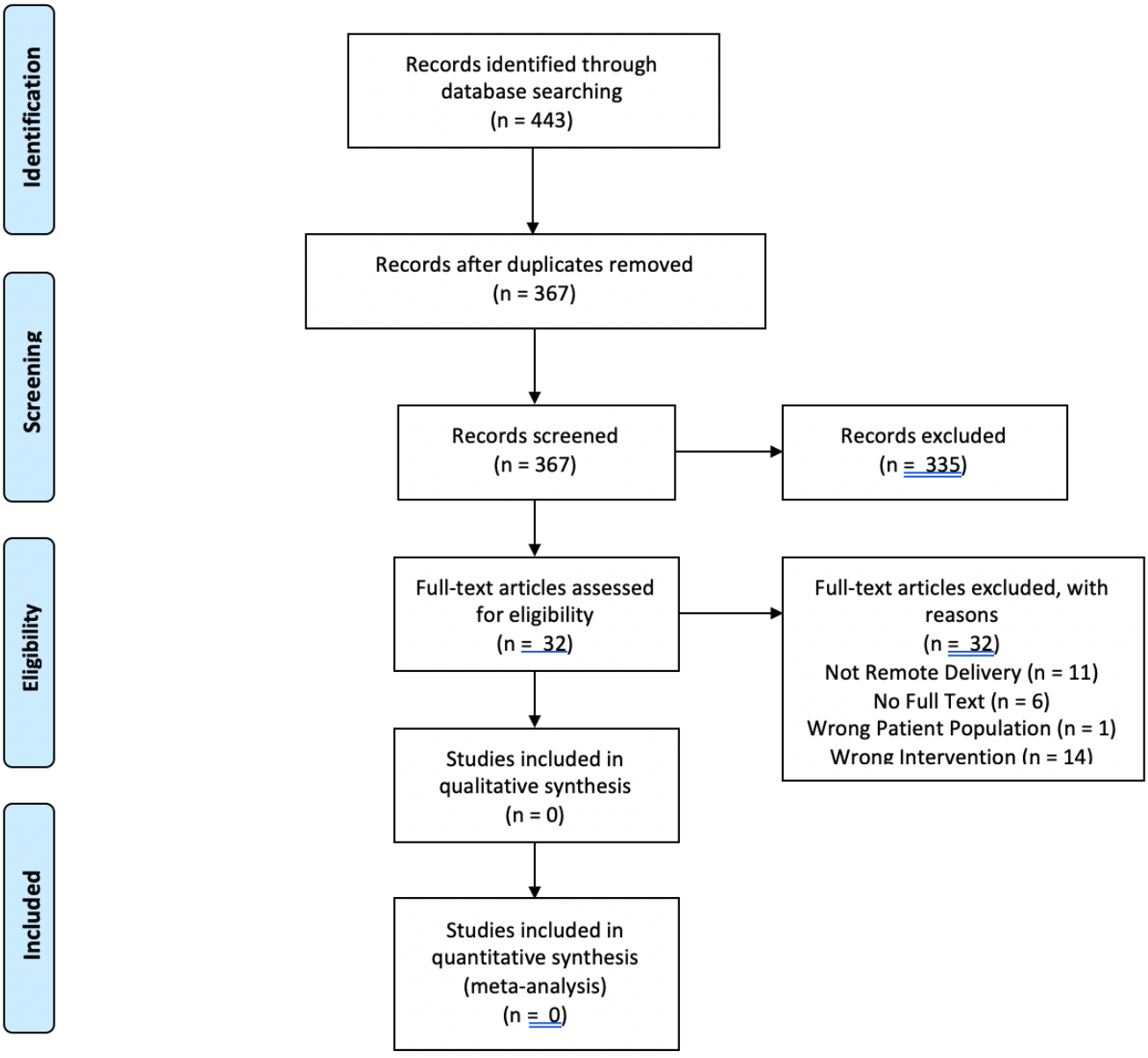
Illness Management and Recovery



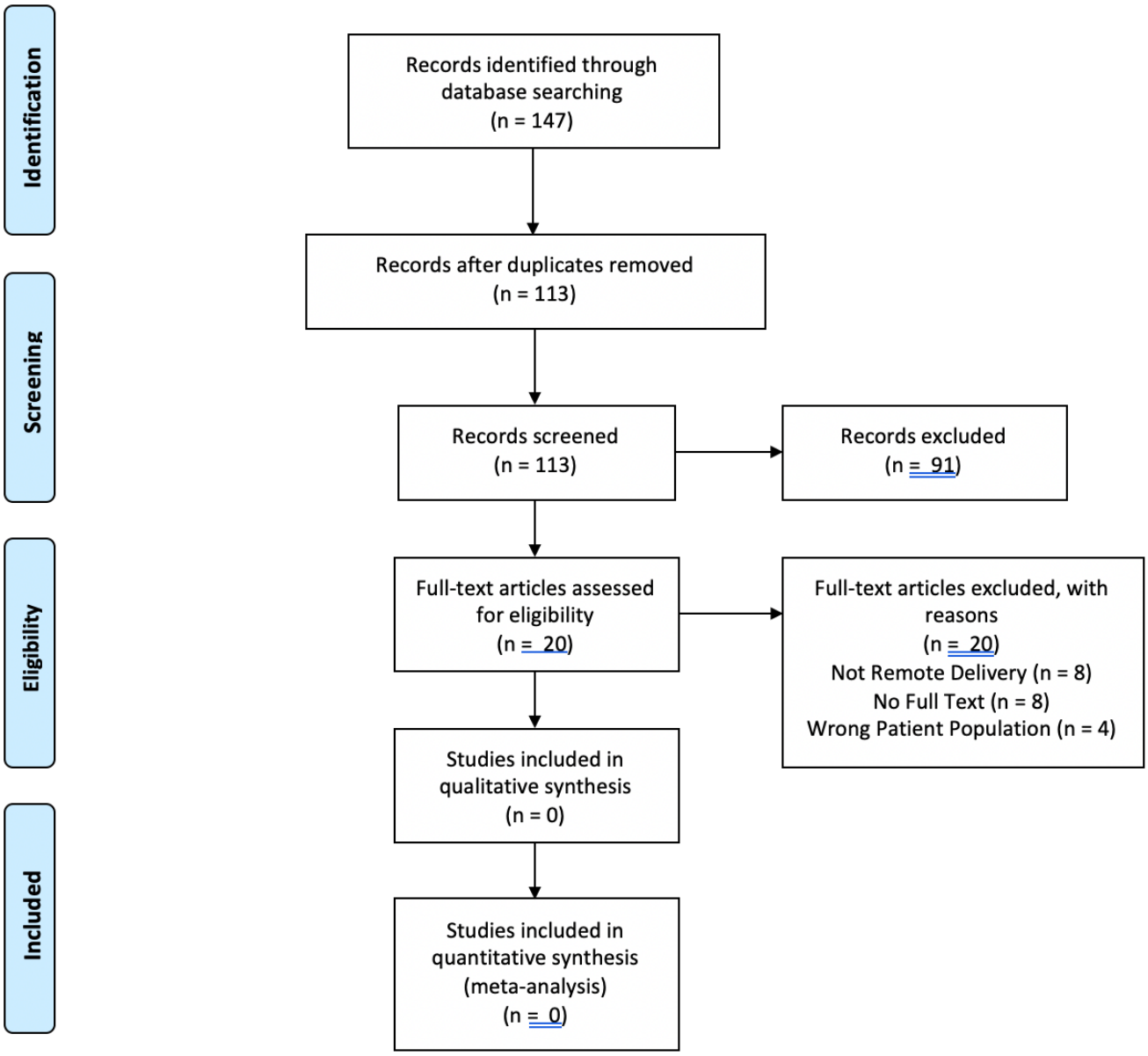
Social Learning / Token Economy



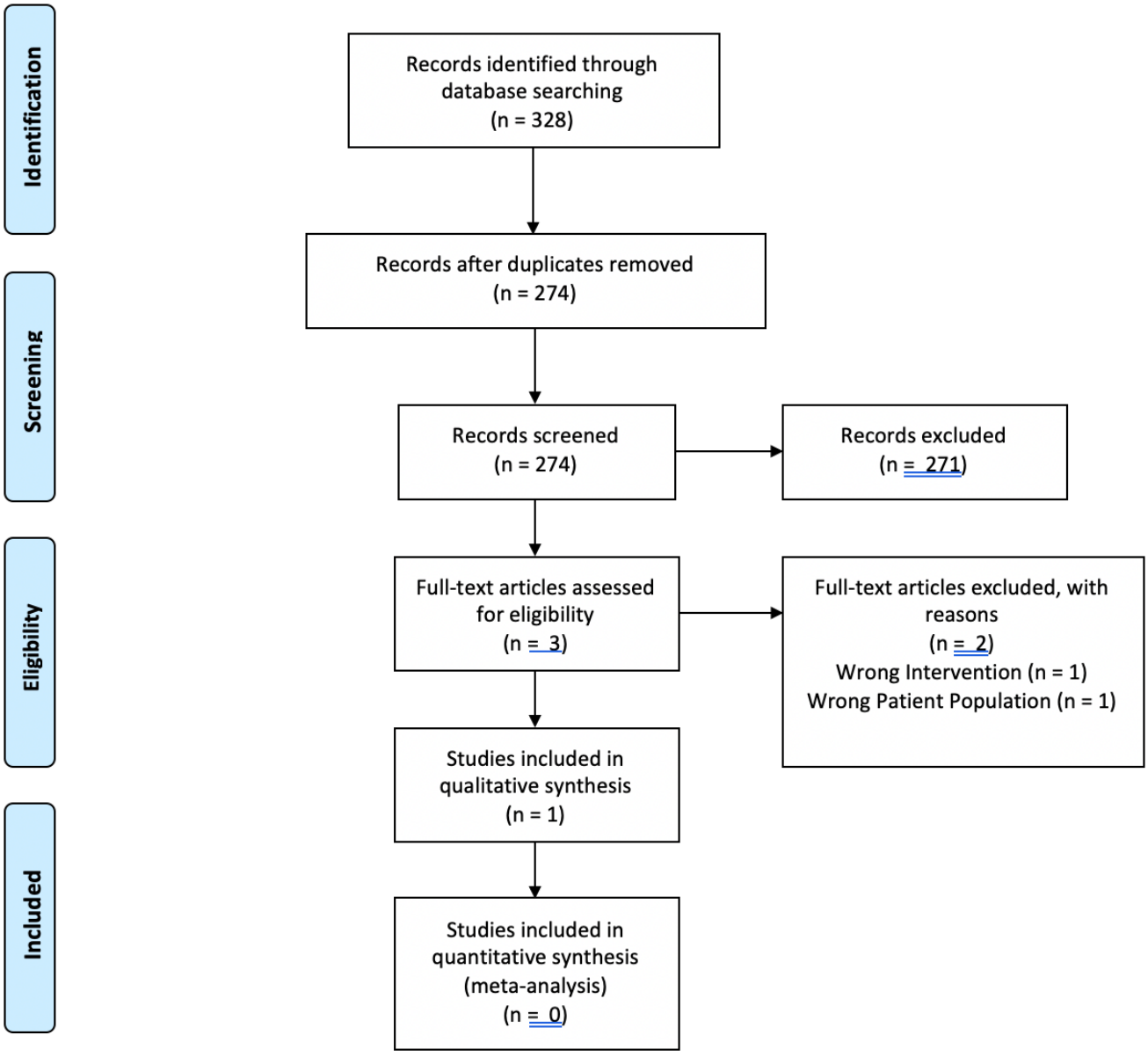
Social Skills Training



Supported Employment



Acceptance and Commitment Therapy



APPENDIX B: List of Included Articles

Cognitive Behavioural Therapy	
Granholm et al. (2012)	MATS App
Alvarez-Jimenez et al. (2013)	HORYZONS Online Social Therapy
Bucci et al. (2018)	ACTISSIST App
Kim et al. (2018)	Heal Your Mind App
Depp et al. (2019)	CBT2Go App
McEnery et al. (2019)	EMBRACE Online Social Anxiety Therapy
Wilson et al. (2019)	Remote CBT for smoking cessation
Ludwig et al. (2020)	HORYZONS Online Social Therapy
Cognitive Remediation	
Ventura et al. (2013)	Posit Science
Fisher et al. (2015)	Posit Science
Hargreaves et al. (2015)	Working Memory Training
Biagianti et al. (2017)	Posit Science
Harris et al. (2017)	Lumosity, Posit Science, My BrainSolutions, SBTPro
Donohoe et al. (2018)	Working Memory Training
Melo Moura et al. (2019)	COGWEB
Family Psychoeducation	
Rotondi et al. (2005)	Schizophrenia Guide - Telehealth
Glynn et al. (2010)	Psychoeducational website
Rotondi et al. (2010)	Schizophrenia Guide - Telehealth
Haley et al. (2011)	Telepsychiatry education
Hornby et al. (2012)	Web Camera Family Intervention
Hasan et al. (2015)	Booklet psychoeducation
Aschbrenner et al. (2018)	Care2Quit smoking cessation
Illness Management and Recovery	
Ben-Zeev et al. (2018)	FOCUS app
Jonathan et al. (2019)	FOCUS app
Social Learning / Token Economy	
Wilson et al. (2019)	iCOMMIT (smoking cessation app)
Acceptance and Commitment Therapy	
Vilardaga et al. (2019)	Learn to Quit (smoking cessation app)