Data supplement to:

Strategies to prevent death by suicide: a meta-analysis of randomised controlled trials

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British Journal of Psychiatry doi: 10.1192/bjp.bp.116.187799

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Table DS1 Methodological quality and results of trials evaluating suicide prevention strategies[a]

Author, Year	OR (95%CI)	Random sequence generation	Allocation Concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Biases
Cognitive Behavioral Therapies								
Blum, 2008	No events	Low	Unclear	High	Unclear	Unclear	Low	Unclear
Brown, 2005	0.14 (0.00 – 6.82)	Low	Unclear	Unclear	Unclear	Low	Low	Low
Davidson, 2010	0.77 (0.05 – 12.80)	Low	Low	Unclear	Low	Low	Low	Unclear
Davidson, 2014	3.91 (0.05 – 328.91)	Low	Low	Unclear	Unclear	Low	Low	Unclear
Grawe, 2006	No events	Low	Low	High	Unclear	Low	Unclear	Unclear
Hawton, 1987	8.41 (0.17 – 426. 74)	Unclear	Unclear	Unclear	High	Unclear	Unclear	Unclear
Husain, 2014	1.10 (0.15 – 7.93)	Low	Low	Unclear	Unclear	Low	Low	Unclear
Linehan, 1991	6.80 (0.13 – 343.88)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Linehan, 2006	No events	Low	Unclear	High	Unclear	Unclear	Unclear	Unclear
McAuliffe, 2014	0.49 (0.05 – 4.70)	Low	Low	High	Unclear	Unclear	Unclear	High
McMain, 2012	No events	Low	Low	Unclear	Low	Low	Unclear	Unclear
Morley, 2014	No events	Unclear	Low	Unclear	Unclear	Unclear	Unclear	High
Power, 2003	1.00 (0.06 – 16.55)	Unclear	Unclear	Unclear	Low	Low	Unclear	High
Raj, 2001	0.14 (0.00 – 6.82)	High	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Rudd, 1996	No events	Unclear	Unclear	Unclear	Unclear	High	Unclear	Unclear
Rudd, 2015	1.00 (0.06 – 16.14)	Low	Unclear	Unclear	Low	Low	Unclear	Unclear
Slee, 2008	0.14 (0.01 – 2.25)	Low	Low	Unclear	Unclear	Unclear	Low	High
Tarrier, 2006	CBT: 6.84 (0.14 – 345.58) Sup: 6.61 (0.41 – 107.35)	Low	Low	Unclear	High	Unclear	Unclear	Low

Tyrer, 2003	0.43 (0.10 – 1.92)	Low	Unclear	High	Unclear	Low	Low	Unclear
Van Spijker, 2014	No events	Low	Low	High	High	Low	Low	High

OR = Odds Ratio; 95%CI = 95 percent confidence interval; CBT = Cognitive Behavioral Therapy; Sup = Supportive Therapy
a. Based on the Cochrane Risk of Bias Tool; Low = low risk of bias; High = high risk of bias; Unclear= Insufficient evidence to judge risk of bias

Table DS1 Methodological quality and results of trials evaluating suicide prevention strategies[a] (continued)

Author, Year	OR (95% CI)	Random sequence generation	Allocation Concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Biases
Non-Cognitive Behavioral Therapies								
Gregory, 2008	0.14 (0.00 – 6.82)	Low	Unclear	High	Unclear	Low	Unclear	High
Guthrie, 2001	No events	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Gysin-Maillart, 2016	1.00 (0.06 – 16.18)	Low	Low	High	Unclear	Low	Low	Unclear
Winter, 2007	0.83 (0.08 – 8.95)	High	High	Unclear	Unclear	Unclear	Unclear	Unclear
Complex Psychosocial Interventions								
Allard, 1992	2.79 (0.38 – 20.26)	Unclear	Low	High	Low	Low	Unclear	High
Amadeo, 2015	0.12 (0.01 – 1.94)	Low	Unclear	Unclear	Low	Low	Low	Unclear
Bertelsen, 2007	0.59 (0.13 – 2.67)	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Carter, 2005	0.87 (0.26 – 2.85)	Low	Low	High	Low	Low	Unclear	High
Cedereke, 2002	1.07 (0.07 – 17.32)	Unclear	Low	High	Low	Low	Unclear	High
Clarke, 2002	1.12 (0.07 – 18.10)	Low	Unclear	Unclear	Unclear	Low	Unclear	High
Connolly, 1996	1.42 (0.31 – 6.40)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

Dekker, 2002	7.71 (0.48 – 125.04)	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear
De Leo, 2007	No events	Low	Low	High	Unclear	High	Unclear	High
Evans, 1999	1.92 (0.20 – 18.49)	Unclear	Low	Unclear	Low	Low	Unclear	Unclear

OR = Odds Ratio; 95%CI = 95 percent confidence interval
a. Based on the Cochrane Risk of Bias Tool; Low = low risk of bias; High = high risk of bias; Unclear= Insufficient evidence to judge risk of bias

Table DS1 Methodological quality and results of trials evaluating suicide prevention strategies[a] (continued)

	OR (95%CI)	Random sequence generation	Allocation Concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Biases
Complex Psychosocial Interventions (continued)								
Fleischmann, 2008	0.19 (0.08 – 0.45)	Low	Low	Unclear	Unclear	Unclear	Low	Unclear
Grimholt, 2015	1.41 (0.08 – 23.64)	Low	Low	High	Low	Low	Low	High
Hassanian-Moghaddam, 2015	1.95 (0.63 – 6.07)	Low	Low	Unclear	Low	Low	Unclear	Low
Hvid, 2011	1.82 (0.19 – 17.88)	Low	Low	Unclear	Low	Low	Low	High
Kawanishi, 2014	0.88 (0.52 – 1.51)	Low	Low	High	Low	Low	Low	Unclear
Moller, 1992	1.61 (0.27 – 9.52)	High	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Morgan, 1993	No events	Unclear	Low	Unclear	High	Low	Unclear	Unclear
Morthorst, 2012	7.21 (0.14 – 363.52)	Low	Low	Unclear	High	Low	Low	High
Motto, 2001	1.13 (0.64 – 1.99)	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Mouaffak, 2015	7.34 (0.15 – 369.95)	Unclear	Low	High	Low	Low	Unclear	Unclear

Mousavi, 2014	0.29 (0.05 – 1.75)	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Raue, 2010	6.50 (0.13 – 330.64)	Low	Unclear	High	Low	Low	Low	Unclear
Schulberg, 2005	No events	Low	Low	Unclear	Unclear	Low	Unclear	Unclear
Sun, 2012	1.06 (0.15 – 7.76)	Unclear	Low	Unclear	High	High	Unclear	High
Unutzer, 2006	No events	Low	Low	High	Low	Unclear	Low	Unclear
Vaiva, 2006	0.70 (0.07 – 6.99)	Low	Low	High	Low	Low	Unclear	High
Van Heeringen, 1995	0.85 (0.28 – 2.56)	Low	Unclear	Unclear	Low	Low	Unclear	High
Vijayakumar, 2013	0.61 (0.08 – 4.58)	Unclear	Unclear	Unclear	Low	High	Unclear	Unclear
Walsh, 2001	1.23 (0.33 – 4.59)	Unclear	Low	Unclear	High	Low	Unclear	High

OR = Odds Ratio; 95%CI = 95 percent confidence interval
a. Based on the Cochrane Risk of Bias Tool: Low = low risk of bias; High = high risk of bias; Unclear= Insufficient evidence to judge risk of bias

Table DS1 Methodological quality and results of studies evaluating strategies to prevent suicide[a] (continued)

	OR (95%CI)	Random sequence generation	Allocation Concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Biases
Higher Level Care Interventions								
Bateman, 2008	0.12 (0.00 – 5.89)	Unclear	Unclear	High	High	Unclear	Unclear	Unclear
Jones, 2008	0.40 (0.02 – 8.21)	High	Low	High	Low	Low	Unclear	High
Van Der Sande, 1997	0.49 (0.05 – 4.74)	Low	Low	Unclear	Low	Low	Unclear	Unclear
Somatic Therapies								
George, 2014	No events	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear

Nordenskjold, 2013	0.14 (0.00 – 6.82)	Low	Low	Unclear	Unclear	Low	Unclear	High
Randomized Controlled Trials of Medications								
Antidepressants								
Hirsch, 1982	No events	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Montgomery, 1983	No events	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear
Nelson, 2007	No events	Unclear	Unclear	Low	Low	Low	Unclear	Unclear
Phillips, 2009	No events	Low	Low	Low	Unclear	Unclear	Unclear	Unclear
Rosenthal, 2013	No events	Low	Low	Low	Unclear	Low	Low	Unclear
Verkes, 1998	0.13 (0.00 – 6.67)	Unclear	Unclear	Low	Unclear	Low	Low	Low
Zisook, 2011	No events	Unclear	Unclear	Low	Low	Low	Unclear	Unclear
Mood Stabilizers								
Bauer, 2000	0.14 (0.00 – 7.31)	Unclear	Unclear	Low	Unclear	Low	Unclear	Unclear
Girlanda, 2014	6.44 (0.13 – 327.93)	Low	Low	Unclear	Unclear	High	Low	High
Khan, 2011	No events	Low	Low	Low	Unclear	Low	Low	Low
Lauterbach, 2008	0.13 (0.01 – 1.27)	Low	Unclear	Low	Unclear	Unclear	Low	High

OR = Odds Ratio; 95%CI = 95 percent confidence interval
a. Based on the Cochrane Risk of Bias Tool: Low = low risk of bias; High = high risk of bias; Unclear= Insufficient evidence to judge risk of bias

Table DS1 Methodological quality and results of studies evaluating strategies to prevent suicide[a] (continued)

	OR (95% CI)	Random sequence generation	Allocation Concealment	Blinding of participants & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Biases
Mood Stabilizers (continued)								
Prien, 1973a	0.12 (0.00 – 5.91)	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear
Prien, 1973b	0.14 (0.00 – 7.02)	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear
Nutritional Supplement								
Hallahan, 2007	No events	Low	Low	Low	Unclear	Low	Unclear	Unclear
Pooled Analysis of Randomized Controlled Trials of Medications[b]								
Antidepressants								
Aursnes, 2005	n/a	Low	Low	Low	Low	Low	Unclear	Low
Hammad, 2006	n/a	Low	Low	Low	Low	Low	Unclear	Low
Khan, 2007	n/a	Low	Low	Low	Low	Low	Unclear	High
Antipsychotics								
Khan, 2013	n/a	Low	Low	Low	Low	Low	Unclear	High
Storosum, 2003	n/a	Low	Low	Low	Low	Low	Unclear	Low
Mood Stabilizers								
Storosum, 2005	n/a	Low	Low	Low	Low	Low	Unclear	Low

OR = Odds Ratio; 95%CI = 95 percent confidence interval; N/A = not applicable

a. Based on the Cochrane Risk of Bias Tool; Low = low risk of bias; High = high risk of bias; Unclear= Insufficient evidence to judge risk of bias
b. Peto odds ratios could not be calculated for the results of individual pooled analysis of randomized controlled trials due to large imbalances in treatment arms.

Table DS2 Incidence rate ratios of death by suicide for various suicide prevention strategies[a]

Intervention domain	N	IRR	95% Confidence Interval
Complex Psychosocial Interventions	29	0.93	0.65 – 1.33
Intensive follow-up programs	11	0.71	0.34 – 1.48
Comprehensive follow-up programs	5	0.30	0.07 – 1.22
Case management after suicidal behavior	4	0.93	0.56 – 1.54
Case management for psychosis	4	1.16	0.50 – 2.55
Letter/Phone Contact	7	1.16	0.75 – 1.79
Psychotherapy[b]	24	0.79	0.41 – 1.53
Cognitive Behavioral Therapies	20	0.72	0.34 – 1.53
Cognitive Behavioral Therapy-Suicide Prevention	6	0.30	0.08 – 1.11

Problem Solving Therapy	4	1.00	0.25 – 4.04
Non-Cognitive Behavioral Therapies	5	1.10	0.27 – 4.38
Medications (Randomized Trials)	14	0.10	0.00 – 32.27
Lithium	6	0.14	0.00 – 9.41
Medications (Pooled Analysis)	6	1.15	0.56 – 2.39

IRR = incidence rate ratio; N = number of studies

a. There were too few studies to calculate IRR for the following domains: means restriction; cognitive behavioral therapies (except for cognitive behavioral therapy designed to address suicidal behavior and problem solving therapy); non-cognitive behavioral therapies; aftercare; other types of intensive follow-up programs, primary mental health integrated care; nursing-led caregiver education; higher-level care; somatic therapies, and medications by type (except for lithium).

b. A third arm of the CBT trial conducted by Tarrier *et al* (online supplemental references[107]) evaluated supportive therapy for psychosis. This arm was included in the analysis of non-CBT therapies.

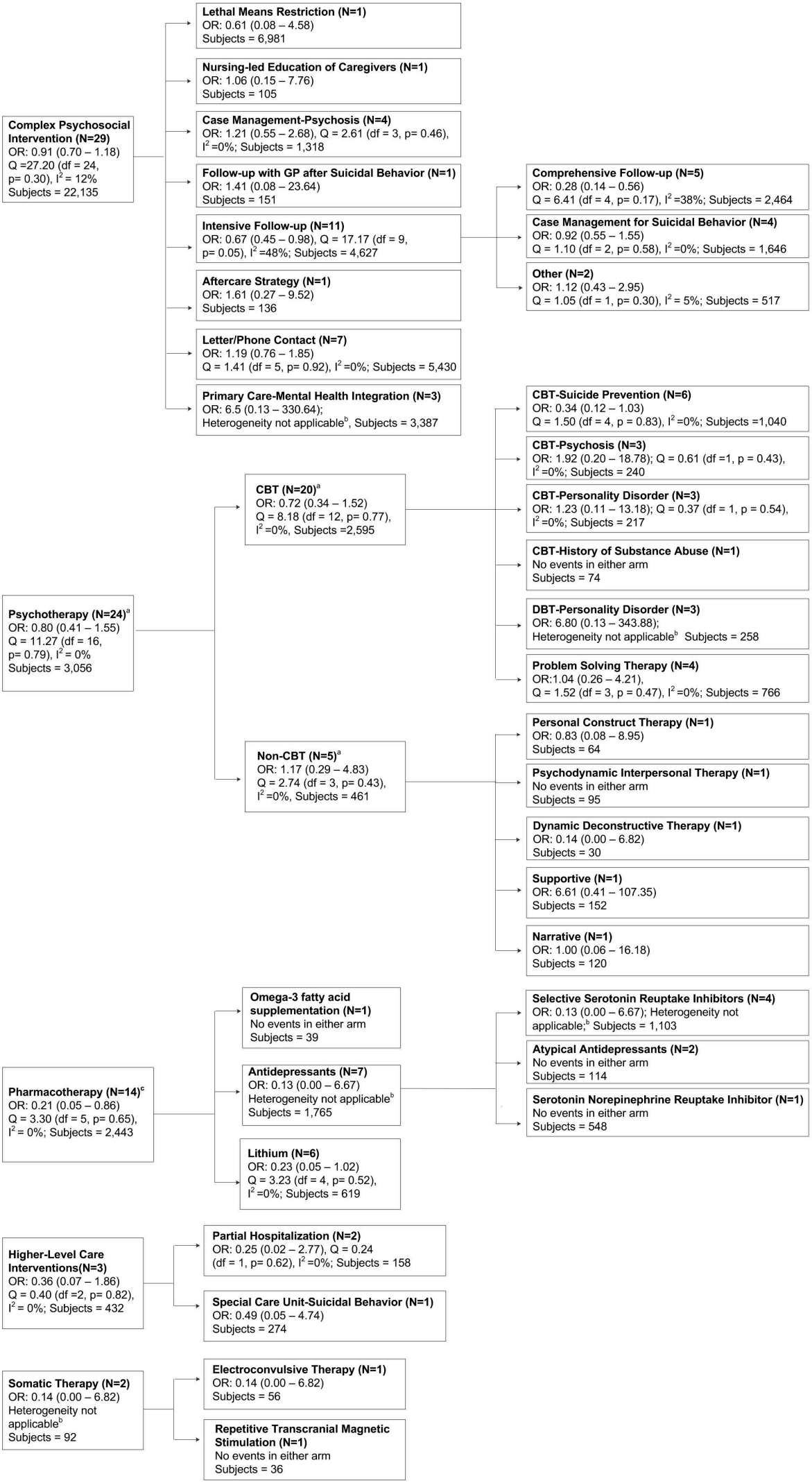
Complex Psychosocial Intervention (N=29)
OR: 0.91 (0.70 – 1.18)
Q =27.20 (df = 24, p= 0.30), I² = 12%
Subjects = 22,135
Lethal Means Restriction (N=1)
OR: 0.61 (0.08 – 4.58)
Subjects = 6,981
Nursing-led Education of Caregivers (N=1)
OR: 1.06 (0.15 – 7.76)
Subjects = 105
Case Management-Psychosis (N=4)
OR: 1.21 (0.55 – 2.68), Q = 2.61 (df = 3, p= 0.46), I² =0%; Subjects = 1,318
Follow-up with GP after Suicidal Behavior (N=1)
OR: 1.41 (0.08 – 23.64)
Subjects = 151
Intensive Follow-up (N=11)
OR: 0.67 (0.45 – 0.98), Q = 17.17 (df = 9, p= 0.05), I² =48%; Subjects = 4,627
Comprehensive Follow-up (N=5)
OR: 0.28 (0.14 – 0.56)
Q = 6.41 (df = 4, p= 0.17), I² =38%; Subjects = 2,464
Case Management for Suicidal Behavior (N=4)
OR: 0.92 (0.55 – 1.55)
Q = 1.10 (df = 2, p= 0.58), I² =0%; Subjects = 1,646
Other (N=2)
OR: 1.12 (0.43 – 2.95)
Q = 1.05 (df = 1, p= 0.30), I² = 5%; Subjects = 517
Aftercare Strategy (N=1)
OR: 1.61 (0.27 – 9.52)
Subjects = 136
Letter/Phone Contact (N=7)
OR: 1.19 (0.76 – 1.85)
Q = 1.41 (df = 5, p= 0.92), I² =0%; Subjects = 5,430
Primary Care-Mental Health Integration (N=3)
OR: 6.5 (0.13 – 330.64);
Heterogeneity not applicable[b], Subjects = 3,387
Psychotherapy (N=24)[a]
OR: 0.80 (0.41 – 1.55)
Q = 11.27 (df = 16, p= 0.79), I² = 0%
Subjects = 3,056
CBT (N=20)[a]
OR: 0.72 (0.34 – 1.52)
Q = 8.18 (df = 12, p= 0.77), I² =0%, Subjects =2,595
CBT-Suicide Prevention (N=6)
OR: 0.34 (0.12 – 1.03)
Q = 1.50 (df = 4, p = 0.83), I² =0%; Subjects =1,040
CBT-Psychosis (N=3)
OR: 1.92 (0.20 – 18.78); Q = 0.61 (df =1, p = 0.43), I² =0%; Subjects = 240
CBT-Personality Disorder (N=3)
OR: 1.23 (0.11 – 13.18); Q = 0.37 (df = 1, p = 0.54), I² =0%; Subjects = 217
CBT-History of Substance Abuse (N=1)
No events in either arm
Subjects = 74
DBT-Personality Disorder (N=3)
OR: 6.80 (0.13 – 343.88);
Heterogeneity not applicable[b] Subjects = 258
Problem Solving Therapy (N=4)
OR:1.04 (0.26 – 4.21),
Q = 1.52 (df = 3, p = 0.47), I² =0%; Subjects = 766
Non-CBT (N=5)[a]
OR: 1.17 (0.29 – 4.83)
Q = 2.74 (df = 3, p= 0.43), I² =0%, Subjects = 461
Personal Construct Therapy (N=1)
OR: 0.83 (0.08 – 8.95)
Subjects = 64
Psychodynamic Interpersonal Therapy (N=1)
No events in either arm
Subjects = 95
Dynamic Deconstructive Therapy (N=1)
OR: 0.14 (0.00 – 6.82)
Subjects = 30
Supportive (N=1)
OR: 6.61 (0.41 – 107.35)
Subjects = 152
Narrative (N=1)
OR: 1.00 (0.06 – 16.18)
Subjects = 120
Pharmacotherapy (N=14)[c]
OR: 0.21 (0.05 – 0.86)
Q = 3.30 (df = 5, p= 0.65), I² = 0%; Subjects = 2,443
Omega-3 fatty acid supplementation (N=1)
No events in either arm
Subjects = 39
Antidepressants (N=7)
OR: 0.13 (0.00 – 6.67)
Heterogeneity not applicable[b]
Subjects = 1,765
Selective Serotonin Reuptake Inhibitors (N=4)
OR: 0.13 (0.00 – 6.67); Heterogeneity not applicable;[b] Subjects = 1,103
Atypical Antidepressants (N=2)
No events in either arm
Subjects = 114
Serotonin Norepinephrine Reuptake Inhibitor (N=1)
No events in either arm
Subjects = 548
Lithium (N=6)
OR: 0.23 (0.05 – 1.02)
Q = 3.23 (df = 4, p= 0.52), I² =0%; Subjects = 619
Higher-Level Care Interventions(N=3)
OR: 0.36 (0.07 – 1.86)
Q = 0.40 (df =2, p= 0.82), I² = 0%; Subjects = 432
Partial Hospitalization (N=2)
OR: 0.25 (0.02 – 2.77), Q = 0.24 (df = 1, p= 0.62), I² =0%; Subjects = 158
Special Care Unit-Suicidal Behavior (N=1)
OR: 0.49 (0.05 – 4.74)
Subjects = 274
Somatic Therapy (N=2)
OR: 0.14 (0.00 – 6.82)
Heterogeneity not applicable[b]
Subjects = 92
Electroconvulsive Therapy (N=1)
OR: 0.14 (0.00 – 6.82)
Subjects = 56
Repetitive Transcranial Magnetic Stimulation (N=1)
No events in either arm
Subjects = 36

Fig. DS1

Appendix DS1

Title: Strategies to prevent death by suicide: a meta-analysis of randomized controlled trials

Authors: Riblet NB, Shiner B, Young-Xu Y, Watts BV

Introduction:

Suicide is a significant public health concern in the United States. The Centers for Disease Control estimates that over 30,000 people die by suicide each year in the U.S.[1] Suicide is also the tenth leading cause of death among people of all ages[1] and the third leading cause of death among adolescents ages 15 to 24 years old.[1] Suicidal behavior is associated with significant costs to society with an estimated annual loss of 34.6 billion dollars due to healthcare costs and lost earnings.[2] Caring for a loved one who is suicidal can also cause considerable emotional toll on family members and loved ones.[3]

Although many strategies have been proposed to prevent suicide, the efficacy of these various interventions remains unclear.[4-5] For example, antidepressants may have a protective effect in mood disorders but these findings are largely based on studies which are underpowered and of short duration.[5] Similarly, it is unclear whether antipsychotics or mood stabilizers have an anti-suicidal effect.[5] The role of behavioral interventions and more comprehensive suicide prevention programs in reducing suicide also remains unclear. Safer packaging of medications has shown some promise but these studies may be limited by confounding and inadequate duration.[6]

In 2005, Mann *et al* published a comprehensive systematic review of all available suicide prevention strategies.[7] These authors concluded that there was evidence to support the following interventions including physician education in depression recognition, gatekeeper education and lethal means restriction.[7] The authors, however, determined that the efficacy of individual components of multifaceted strategies for suicide prevention remains unclear.[7]

Since Mann *et al's* review, there have been several additional studies of suicide prevention interventions. These studies continue to produce mixed results. For example, a randomized controlled trial of a worldwide disseminated gatekeeper training called ASIST found that there was no significant improvement in gatekeeper knowledge about suicide prevention with this training.[8] On the other hand, a randomized controlled trial of a brief psychological intervention after self harm found that the therapeutic intervention was associated with a significant (and sustained) reduction in symptoms of suicidal ideation.[9]

Our current review provides an update to the previous comprehensive systematic review completed by Mann *et al* in 2005.[7] We have used the conceptual framework previously developed by Mann *et al* to understand and to evaluate existing strategies for suicide prevention.[7] Our aim is to provide a complete and all-inclusive summary of all of the available evidence for interventions to prevent suicide. We believe that this information will help inform clinical decisions about suicide prevention and illuminate areas in need of additional research.

Research Question: Among adults 18 years and older (P), which interventions that are designed to prevent death by suicide (or suicidal behavior or ideation) (I) have greater efficacy than usual care condition, placebo or waitlist (C) at preventing death by suicide (O)?

STUDY INCLUSION CRITERIA

Inclusion Criteria Table & Outcomes of Interest:

Category	**Inclusion Criteria**	**Justification/Explanation**	**Order**
Study Design:	Randomized Controlled Trials (RCTs), pooled analysis of RCTs	While RCTs are not ideal for studying a rare outcome such as death by suicide, we will limit our review to this study design because RCTs are the highest quality study design and the gold standard for evaluating the efficacy of an intervention.[10-11] We will also	1

		include the results of pooled analysis of RCTs of pharmacological interventions to better understand the role of medications in preventing death by suicide. We have chosen this approach because death by suicide is a rare outcome and individual drug trials are unlikely to be powered to evaluate for this particular outcome but pooled analysis using a systematic approach to identify death by suicide in drug trials may offer unique insights.	
Population	Any adult age 18 and older	Since the risk for death by suicide spans all types of adult populations and covers a wide range of risk factors (e.g. known mental health problems, access to lethal means, Veteran status), we plan to broaden our population to include interventions targeted at reducing risk for suicide in all adults over the age of 18. [11] In order to be comprehensive and include as many studies as possible, we will include studies if the total population (or the large majority) was 18 years and older. We have decided to exclude children and adolescents from our review since this population may have uniquely different	2

		responses to potential therapeutic interventions to prevent death by suicide. Therefore, a comprehensive review of interventions to prevent death by suicide in the child/adolescent population would be warranted but is beyond the scope of the current review.	
Intervention:	Interventions targeted at preventing death by suicide (or suicidal behavior or ideation) in a population	We will use a framework based on the work presented by Mann *et al's* in their systematic review of the literature.[7] These interventions fall into the following major categories:[7] 1) Education and Awareness Programs 2) Screening for individuals at high risk 3) Pharmacotherapy 4) Psychotherapy 5) Follow-up Care for Suicide Attempts 6) Restriction of Access to Lethal Means 7) Media Reporting Guidelines for suicide If necessary, we will create additional domains and sub-domains (or remove domains) based on consensus if we identify new interventions which were not covered in Mann *et al's* review and do not readily fit into the domains developed in their review or we identify that there are certain domains	3

		which were not studied using a randomized design methodology.[7]	
Comparison	Usual care or placebo condition (placebo or sham) or waitlist	Since the primary concern in the literature is whether any suicide prevention strategies are effective, we will include as our comparator arm usual care condition or placebo or waitlist. Usual care may include any intervention that would be considered standard of care based on current clinical practice and would be unethical to withhold from a patient. This may include typical supportive care interventions such as routine visits with a physician and provider education as well as allowing patients to seek out psychotherapy or continue taking pharmacological agents. Similarly, we will allow waitlist comparison. We will also allow the comparison arm to include placebo or sham as this would be relevant (and expected) in the case of pharmacotherapy trials or somatic therapies such as electroconvulsive therapy and transcranial magnetic stimulation. Since there is limited knowledge about the efficacy of any available interventions to prevent death by	4

		suicide, we have not included active treatment as a comparison. The aim of this review is to identify which interventions are superior to standard treatment. Our review will not address issues of equivalency or non-inferiority. We will, however, briefly summarize in a qualitative fashion the results of trials that evaluate active treatment as comparison.	
Outcomes:	Death by suicide	We will require that included studies report on death by suicide. While studies are more likely to report on intermediary outcomes such as suicidal behavior or suicidal ideation, these outcomes are known to be more susceptible to measurement bias.[12] Furthermore, it is clear that from a societal perspective the prevention of death by suicide is the most relevant clinical outcome.[1-2] To broaden our search and be as inclusive as possible, we will include studies that report death by suicide as a primary outcome or a secondary outcome. In the event that death suicide was a secondary outcome, we will require that the primary aim of the report included the prevention of	5

		suicidal ideation and/or suicidal behavior. We have selected this method to help minimize biases due to the fact that these studies will be far less likely to be powered to evaluate for death by suicide. In addition, we will exclude a study if they do not clearly state whether or not death by suicide occurred in one or both arms (i.e. we will not assume that no mention of death by suicide means no death by suicide occurred). However, to be as inclusive as possible, we will include studies even if the methods that they used to assess for death by suicide were at higher risk for bias (e.g. informants, chart review). Finally, given that death by suicide is a rare outcome, we will include studies even if they report that no events (death by suicide) occurred in either arm.	

Outcomes of Interest:

Primary Outcome:

Odds of death by suicide

Justification: This is the most relevant question with regards to whether suicide prevention strategies are effective.[1-2]

Search Strategy:

Databases:

We used the following databases for our review including Medline (via Ovid), the Cochrane Library, PsycINFO, Excerpta Medica Database (EMBASE) and The Cumulative Index to Nursing and Allied Health Literature (CINAHL).

Search terms:

We used exploded MeSH terms and key words to generate the following themes: suicide, prevention and control and treatment. We then used "OR" to combine the theme prevention and control and treatment and the Boolean term "AND" to find their intersection with the theme suicide (see search strategy below). We applied this approach during our search of the Medline database and modified our approach as necessary to search the Cochrane Library, PsycINFO, EMBASE, CINAHL and clinicaltrials.gov.

Limits:

We applied a randomized controlled trial limit in our search of the Cochrane Library.

Special Strategies:

We applied Cochrane's recommended highly sensitive search strategy for identifying randomized controlled trials in our Medline, EMBASE and PsycINFO search because our original search yielded an unfeasible number of studies to search manually.[13-16] Similarly, we applied a sensitive search strategy for identifying randomized controlled trials in CINAHL recommended by the Scottish Intercollegiate Guidelines Network.[17]

Results of Search Strategy:

Using the above search terms, we identified 11,866 potentially eligible studies through our electronic database searching. Details of the structure and findings of our various search strategies are provided below (see search strategy).

Additional Search methods:

In order to identify relevant published and unpublished studies which may have been missed in our preliminary search, we searched clinicaltrials.org and manually reviewed

references of relevant articles. The results of our clinicaltrials.gov search and reference review are provided below (see search strategy).

Prior Reviews:

There have been several prior reviews of this topic both in the general population as well as in specific subpopulations such as Veterans.[4-7] The most recent comprehensive systematic review that has been published, however, was the review undertaken by Mann *et al* in 2005.[7] We feel that updating the work of Mann *et al* is important since there have been several additional randomized controlled trials which have been published since 2005 which may help shed additional light on this topic.[8-9]

Results of Preliminary Search

We have provided an example of an abstract that we located during our initial search which meets all of our inclusion criteria (see preliminary abstracts).

Protocol Amendments:

Since our protocol was written, we have made one amendment. Please see the protocol amendments section below for further details.

Search Terms Table

Theme	MeSH Terms	Key Words
Suicide	Suicidal Ideation, Suicide, Attempted, Suicide	Suicide
Prevention and control	Health education, Health promotion, mass screening, risk assessment, school health services, student health services, firearms, gas poisoning, pesticides, drug overdose, mass media, harm reduction, emergency services, hospital,	Health education, Health promotion, Mass screening, risk assessment, school health services, student health services, firearms, gas poisoning, pesticide, drug overdose, mass media, harm reduction, emergency service hospital, means restriction, restricted access, media, suicide prevention pc.fs (free floating subheading of prevention & control)
Treatment	antidepressive agents/pd [pharmacology], serotonin uptake inhibitors, antipsychotic agents/pd [pharmacology], psychotropic drugs/pd [pharmacology], antimanic agents/pd [pharmacology], electroconvulsive therapy, monoamine oxidase inhibitors/pd [pharmacology], psychotherapy, cognitive therapy, transcranial magnetic stimulation, ketamine, vagus nerve stimulation, transcutaneous electric nerve stimulation	serotonin uptake inhibitors, ECT, TCA, SSRI, MAOI, CBT, rTMS, ketamine, VNS, vagus nerve stimulator, TENS

Search Strategy

Database: Ovid MEDLINE(R) inception (1945) to Present (December 31, 2015)
The search strategy was created with assistance from a Librarian at the Dartmouth Hitchcock Medical Library

Number	Search terms
1	Suicide.mp or exp Suicide/ or exp Suicide, Attempted/
2	Suicidal ideation.mp or exp Suicidal Ideation/
3	1 or 2
4	Health education.mp or exp Health Education/
5	Health promotion.mp or exp Health Promotion/
6	Mass screening.mp or exp Mass Screening/
7	Risk assessment.mp or exp Risk Assessment/
8	Student health services.mp or exp Student Health Services/
9	Firearms.mp or exp Firearms/
10	Gas poisoning.mp or exp Gas Poisoning/
11	Pesticides.mp or exp Pesticides/
12	Drug overdose.mp or exp Drug Overdose/
13	Mass media.mp or exp Mass Media/
14	Harm reduction.mp or exp Harm Reduction/
15	Emergency service hospital.mp or exp Emergency Service, Hospital/
16	Means restriction.mp
17	Restricted access.mp
18	Media.mp
19	Suicide prevention.mp
20	Exp Antidepressive Agents/pd [Pharmacology/]
21	Exp Serotonin Uptake Inhibitors/pd [Pharmacology/]
22	Serotonin uptake inhibitors.mp
23	Exp Antipsychotic Agents/pd [Pharmacology/]
24	Exp Psychotropic Drugs/pd [Pharmacology/]
25	Exp Antimanic Agents/pd [Pharmacology/]
26	Exp Electroconvulsive Therapy/ or ECT.mp

27	Exp Monoamine Oxidase Inhibitors/pd [Pharmacology/]
28	Exp Psychotherapy/
29	Exp Cognitive Therapy/
30	TCA.mp
31	SSRI.mp
32	MAOI.mp
33	CBT.mp
35	Exp Transcranial Magnestic Stimulation/ or rTMS.mp
36	Ketamine.mp or exp.Ketamine/
37	VNS.mp or exp Vagus Nerve Stimulation/
38	Exp Transcutaneous Electric Nerve Stimulation/
39	Vagus nerve stimulator.mp
40	TENS.mp
41	Pc.fs
42	4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41
43	3 and 42 (Citations located = 21,469)
44	(randomized controlled trial.pt OR controlled clinical trial.pt OR randomized.ab OR placebo.ab OR drug therapy.fs. OR randomly.ab OR trial.ab OR groups.ab)
45	Exp animals/not humans.sh
46	#44 NOT #45
47	46 and 43 (Citations located = 4,641)

*Of note we applied Cochrane's recommended highly sensitive search strategy for identifying randomized controlled trials (Line 44, 45, 46) because our original search yielded unfeasible number of studies to search manually.[13]

EMBASE Search:

Dates Searched: Inception thru December 31, 2015

Search terms were adapted from our Medline search to conform with Emtree and applied as follows: (Suicide OR Suicidal Ideation OR Suicide Attempt) AND (health education OR health promotion OR mass screening OR risk assessment OR health service OR firearms OR gas poisoning OR pesticide OR drug overdose OR mass media OR harm reduction OR emergency health service OR means restriction OR restricted access OR media OR suicide prevention OR suicide prevention and control OR antidepressive agents OR serotonin uptake inhibitor OR neuroleptic agent OR psychotropic drugs OR tranquilizer OR electroconvulsive therapy OR monoamine oxidase inhibitor OR psychotherapy OR cognitive therapy OR TCA OR SSRI OR MAOI OR CBT OR transcranial magnetic stimulation OR ketamine OR rTMS OR VNS OR vagus nerve stimulation OR vagus nerve stimulator OR transcutaneous nerve stimulation OR TENS) AND (random$ OR factorial$ OR crossover$ OR cross over$ OR cross-over$ OR placebo$ OR doubl$ adj blind$ OR singl$ adj blind$ OR assign$ OR allocat$ OR volunteer$ OR crossover-procedure OR double-blind procedure OR randomized controlled trial OR single-blind procedure)

Search Strategy: We used the same search approach as described in our search of Medline but as described above modified the search to conform with Emtree. Furthermore, because our original search yielded an unfeasible number of citations to search by hand, we applied a sensitive search strategy recommended by Cochrane for identifying randomized controlled trials.[14]

Total Citations Located (no limits): 33,832

Total Citations Located (sensitive strategy recommended by Cochrane): 3,297

PsycINFO Search

Dates Searched: Inception thru December 31, 2015

Search Terms: (Suicide OR Suicidal Ideation OR Suicide Attempt) AND (health education OR health promotion OR mass screening OR risk assessment OR student health services OR firearms OR gas poisoning OR pesticides OR drug overdose OR mass media OR harm reduction OR emergency service hospital OR means restriction OR restricted access OR media OR suicide

prevention OR antidepressive agents OR serotonin uptake inhibitors OR antipsychotic agents OR psychotropic drugs OR antimanic agents OR electroconvulsive therapy OR monoamine oxidase inhibitors OR psychotherapy OR cognitive therapy OR SSRI OR MAOI OR CBT OR TCA OR transcranial magnetic stimulation OR ketamine OR rTMS OR VNS OR vagus nerve stimulation OR vagus nerve stimulator OR transcutaneous electric nerve stimulation OR TENS) AND (SU.EXACT ("Treatment Effectiveness Evaluation") OR SU.EXACT.EXPLODE ("Treatment Outcomes") OR SU.EXACT("Placebo") OR SU.EXACT("Followup Studies") OR placebo* OR random* OR "comparative stud*" OR clinical NEAR/3 trial* OR research NEAR/3 design OR evaluat* NEAR/3 stud* OR prospectiv* NEAR/3 stud* OR (singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*))

Search Strategy: We used the same search approach as described in our search of Medline. We applied a sensitive search strategy recommended by Cochrane for identifying randomized controlled trials in PsycINFO.[15-16]

Total Citations Located (no limits)—19,592

Total Citations Located (with sensitive search strategy recommended by Cochrane)---1,525

CINAHL Search:

Dates Searched: Inception thru December 31, 2015

Search Terms: (Suicide OR Suicidal Ideation OR Suicide Attempt) AND (health education OR health promotion OR mass screening OR risk assessment OR student health services OR firearms OR gas poisoning OR pesticides OR drug overdose OR mass media OR harm reduction OR emergency service hospital OR means restriction OR restricted access OR media OR suicide prevention OR antidepressive agents OR serotonin uptake inhibitors OR antipsychotic agents OR psychotropic drugs OR antimanic agents OR electroconvulsive therapy OR monoamine oxidase inhibitors OR psychotherapy OR cognitive therapy OR SSRI OR MAOI OR CBT OR TCA OR transcranial magnetic stimulation OR ketamine OR rTMS OR VNS OR vagus nerve stimulation OR transcutaneous electric nerve stimulation OR vagus nerve stimulator OR TENS) and ((MH

"Clinical Trials+") OR PT Clinical Trial OR TX clinic* n1 trial* OR (TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) OR TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*)) OR TX randomi* control* trial* OR (MH "Random Assignment") OR TX random* allocate* OR TX placebo* OR (MH "Placebos") OR (MH "Quantitative Studies") or TX allocate* random*)

Search strategy: We used the same search approach as described in our search of Medline. We then applied a search filter limit to identify randomized trials recommended by the Scottish Intercollegiate Guidelines Network.[17]

Total Citations Located (no limits)—8,212

Total Citations Located (with sensitive search strategy from SIGN)--- 2,171

Cochrane Library Search:

Dates Searched: Inception thru December 31, 2015

Search Strategy: Search Terms: (Suicide OR Suicidal Ideation OR Suicide Attempt) AND (health education OR health promotion OR mass screening OR risk assessment OR student health services OR firearms OR gas poisoning OR pesticides OR drug overdose OR mass media OR harm reduction OR emergency service hospital OR means restriction OR restricted access OR media OR suicide prevention OR antidepressive agents OR serotonin uptake inhibitors OR antipsychotic agents OR psychotropic drugs OR antimanic agents OR electroconvulsive therapy OR monoamine oxidase inhibitors OR psychotherapy OR cognitive therapy OR SSRI OR MAOI OR CBT OR TCA OR transcranial magnetic stimulation OR ketamine OR rTMS OR VNS OR vagus nerve stimulation OR vagus nerve stimulator OR transcutaneous electric nerve stimulation OR TENS)

Search Strategy: The Cochrane reports that an RCT filter is not required because all the records are thoroughly and correctly indexed. Therefore, we only applied a randomized controlled trial limit in our search.[18]

Total Citations Located (no limits)—2,160

Total Number (with RCT limits applied): 232

Clinical Trials.gov:

Dates: Inception thru December 31, 2015

Search Strategy: "suicide & prevention"

Results

- Three trials-no usable data
- Thirteen trials-ongoing/actively recruiting

Reference Review

Additional references located: Three

Preliminary Abstracts

Abstract

Authors: Vijayakumar L, Jeyaseelan L, Kumar S, Mohanraj R, Devika S, Manikandan S. A central storage facility to reduce pesticide suicides--a feasibility study from India. *BMC Public Health* 2013; **13**: 850.

Background: Pesticide suicides are considered the single most important means of suicide worldwide. Centralized pesticide storage facilities have the possible advantage of delaying access to pesticides thereby reducing suicides. We undertook this study to examine the feasibility and acceptability of a centralized pesticide storage facility as a preventive intervention strategy in reducing pesticide suicides.

Methods: A community **randomized controlled** feasibility study using a mixed methods approach involving a household survey; focus group discussions (FGDs) and surveillance were undertaken. The study was carried out in a district in southern India. Eight villages that engaged in floriculture were identified. Using the lottery method two were randomized to be the **intervention sites** and two villages constituted the **control site**. **Two centralized storage facilities were constructed with local involvement and lockable storage boxes were constructed.** The household survey conducted at baseline and one and a half years later documented information on sociodemographic data, pesticide usage, storage and suicides.

Results: At baseline 4446 individuals (1097 households) in the intervention and 3307 individuals (782 households) in the control sites were recruited while at follow up there were 4308 individuals (1063 households) in the intervention and 2673 individuals (632 households) in the control sites. There were differences in baseline characteristics and imbalances in the prevalence of suicides between intervention and control sites as this was a small feasibility study.The results from the FGDs revealed that most participants found the storage facility to be both useful and acceptable. In addition to protecting against wastage, they felt that it had also helped prevent pesticide suicides as the pesticides stored here were not as easily and readily accessible. The

primary analyses were done on an Intention to Treat basis. Following the intervention, the differences between sites in **changes in combined, completed and attempted suicide rates** per 100,000 person-years were 295 (95% CI: 154.7, 434.8; $p < 0.001$) for pesticide suicide and 339 (95% CI: 165.3, 513.2, $p < 0.001$) for suicide of all methods.

Conclusions: Suicide by pesticides poisoning is a major public health problem and needs innovative interventions to address it. This study, the first of its kind in the world, examined the feasibility of a central storage facility as a means of limiting access to pesticides and, has provided preliminary results on its usefulness. These results need to be interpreted with caution in view of the imbalances between sites. The facility was found to be acceptable, thereby underscoring the need for larger studies for a longer duration.

Confirmation Table

Category	**Inclusion Criteria**	**Criteria Met**
Study Design:	RCTs and pooled analysis of RCTs.	RCT
Population	Any adult age 18 and older	Population in India at risk for suicide including adults
Intervention:	Interventions targeted at preventing death by suicide (or suicidal behavior or ideation) in a population	Centralized storage facility for pesticide
Comparison	Usual care or placebo condition (placebo or sham) or waitlist	Usual care/No storage facility

Outcomes:	Death by suicide	Evaluated death by suicide as an outcome

Protocol Changes

Date **Section of Protocol** Type of amendment*	**Original version**	**New version** Justification
October 15, 2016 Search Strategy -Included additional databases in including EMBASE and CINAHL in addition to Medline, Cochrane Library and PsycINFO -expanded our search terms to include the key word "suicide prevention" in all our electronic database searches (in the case of EMBASE we used suicide prevention as an emtree term). "Suicide prevention" is not a MeSH term in Medline so we could only use it as a keyword. -We used a highly sensitive search strategy recommended by Cochrane to identify RCTs in Medline, EMBASE and PsycINFO. We will use a search strategy for identifying RCTs in	We searched Medline, Cochrane Library, and PsycINFO from inception through December 31, 2015	Based on feedback from reviewers, we added these additional databases and revised our search strategy to increase the likelihood that we would capture all relevant studies. Because we located an unfeasible number of citations to manually search after applying the aforementioned search strategies, we also incorporate recommended highly sensitive search strategy for identifying RCTs in our various electronic searches.

CINAHL recommended by the recommended by the Scottish Intercollegiate Guidelines Network.		

*Amendments may include additions, deletions, changes, and/or clarifications

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18. Cochrane Work. RCT filters for different databases. (http://work.cochrane.org/rct-filters-different-databases)

Appendix DS2

Excluded Studies

Table 1: Randomized trials comparing an intervention versus active control for suicide prevention. (horizontal position)

Author, year	N	Study Population	Study Duration	Intervention	Comparison	Number of suicides by study arm	Study arm favored	Significance
Psychotherapy								
Cottraux, 2008[5]	65	BPD	24 months	Cognitive Therapy	Rogerian Supportive Therapy	No events	Neither	NS
Harned, 2014[1]	26	BPD, PTSD & self-injury	15 months	DBT + PE	DBT	DBT – 1	Neither	NS
Hopko, 2013[4]	80	Breast cancer plus MDD	24 months	Behavioral Activation	PST	No events	Neither	NS
Klingberg, 2012[2]	198	Schizophrenia	12 months	CBT for psychosis	Cognitive remediation	No events	Neither	NS
Linehan, 2015[3]	99	BPD plus ≥2 SA &/or NSSI	24 months	DBT-S	Arm 2: DBT-I Arm 3: Standard DBT	Standard DBT - 1	Neither	NS
Antidepressants								
Perroud, 2009[6]	811	Moderate-Severe Unipolar Depression	3 months	Escitalopram	Nortriptyline	Nortriptyline – 1	Neither	NS

Rucci, 2011[7]	291	Nonpsychotic MDD	4 months	IPT	Escitalopram	No events	Neither	NS
Zisook, 2011[8]	665	Nonpsychotic chronic &/or recurrent MDD	7 months	Escitalopram plus placebo	Arm 2: Bupropion SR plus Escitalopram; Arm3: Venlafaxine XR plus Mirtazapine	No events	Neither	NS
Antipsychotics								
Alphs, 2015[9,a]	450	Schizophrenia & history of incarceration	15 months	Paliperidone palmitate	Daily oral antipsychotics*	No events	Neither	NS
Battaglia, 1999[10,b]	58	Seen in ER after recent SA	6 months	Low dose Fluphenazine decanoate	Ultra-low dose Fluphenazine decanoate	No events	Neither	NS
Buckley, 2015[11,c]	305	Schizophrenia or SCAD	30 months	LAI-R	Physician's choice oral SGA	LAI-R – 1; SGA – 1	Neither	NS
Crespo-Facorro, 2014[12]	202	First Episode Schizophrenia	12 months	Aripiprazole	Arm 2: Ziprasidone Arm 3: Quetiapine	Aripiprazole – 1; Ziprasidone – 1; Quetiapine - 2	Neither	NS
Meltzer, 2003 (InterSePT) [13]	980	Schizophrenia and high risk for suicide	24 months	Clozapine	Olanzapine	Clozapine – 5; Olanzapine – 3	Neither	NS
Strom, 2011[14]	18,154	Schizophrenia (seen in naturalistic practice)	12 months	Ziprasidone	Olanzapine	ITT: RR 1.19 (0.61-2.31) Time on assigned treatment RR: 1.37 (0.66 – 2.85)	Neither	NS

Thomas, 2010[15]	9,858	Schizophrenia	14,147 PY	Sertindole	Risperidone	HR 0.72 (0.36 – 1.41)	Neither	NS
Mood Stabilizers								
Oquendo, 2011[16]	98	Bipolar Disorder plus prior SA	30 months	Lithium	Valproate	Lithium– 0; Valproate - 0	Neither	NS
Thies-Flechtner, 1996[d] (MAP Study) [17]	378	MDD, Bipolar Disorder or SCAD	30 months	Lithium	Arm 2: Amitriptyline; Arm3: Carbamazepine	Lithium– 0; Carbamazepine - 4; Other medications – 5	Lithium	NS

BPD = Borderline Personality Disorder; CBT = Cognitive Behavioral Therapy; DBT = Dialectical Behavior Therapy; DBT-S: DBT skills training; DBT-I: DBT individual therapy; ER = Emergency Room
HR = hazard ratio; IPT = Interpersonal psychotherapy; InterSePT = International Suicide Prevention Trial; ITT = Intention to treat; LAI-R = Long-acting injectable risperidone;
MDD = Major Depressive Disorder; NS = Not statistically significant; NSSI = non-suicidal self-injury; PE = Prolonged exposure; PST = problem solving therapy; PTSD = Post-traumatic stress disorder;
PY = person years; RR = Risk Ratio; SA = Suicide Attempt; SCAD = Schizoaffective Disorder; SGA = Second generation antipsychotics (physician's choice); SR = sustained release; XR = extended

a. Oral antipsychotics may have included aripiprazole, haloperidol, olanzapine, paliperidone, perphenazine, quetiapine, and risperidone
b. Low dose included 12.5 milligram monthly injections of fluphenazine decanoate; Ultra-low dose included 1.5 milligram monthly injections of fluphenazine decanoate
c. SGA may have included aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone, paliperidone, asenapine, and iloperidone
d. The authors report that other medications may have included antidepressants, neuroleptics or no medications

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PRISMA 2009 Checklist Riblet et al. Suicide Prevention Meta-Analysis

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	App 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5-6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5-6

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6-7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7, Table1 eTable2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	eTable2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-9, eTable2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-9, Fig 2 and Fig3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8, eTable2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8-10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097