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1. Introduction

Suicide is a critical global issue. It is the 20th leading cause of death worldwide, with an age-adjusted rate of 16 per 100,000 (World Health Organization). In the United Kingdom, it is estimated that approximately 220,000 patients with self-harm visit hospitals annually (Hawton et al., 2007). The mean number of visits to an emergency department (ED) for attempted suicide and self-inflicted injury per year in the United States was reported as 538,000 in 2005–2008 (Ting et al., 2012).

It is widely recognized that prior suicide attempts and a history of nonsuicidal self-harm are risks for death by suicide and repeat self-harm behavior, including a suicide attempt and nonsuicidal self-harm (Ekeberg et al., 1991; Isometsa and Lonnqvist, 1998; Nielsen et al., 1990; Nordentoft et al., 2011; Nordstrom et al., 1995). Indeed, the risk of a repeat suicide attempt in patients admitted to the ED is as high as 25% (Beautrais, 2004). Previous systematic reviews of psychological autopsy studies revealed that many suicide victims had diagnoses of mental disorders including mood disorders (Arsenault-Lapierre et al., 2004; Bertolote et al., 2004). On the other hand, in our recent article published in the *Journal of Affective Disorders*, we reported that mood disorders were the most frequent psychiatric disorders among suicide attempters in the Emergency Department (Kawashima et al., 2014).

Therefore, the ED is increasingly recognized as an important setting for introducing suicide prevention measures, and studies have focused on developing effective interventions for initiation during an ED stay for patients with attempted suicide (Boudreaux et al., 2013; Hirayasu et al., 2009).

However, recently, inconsistent results were reported between two randomized controlled trials examining the effectiveness of interventions in suicidal patients admitted to the ED (Kapur et al., 2013; Morthorst et al., 2012).

In the present study, we reviewed randomized controlled trials and examined the effects of interventions initiated when suicidal patients were admitted to the ED.

2. Methods

Using an a priori published protocol (Inagaki et al., 2013), we conducted our systematic review and reported according to the criteria of preferred reporting items for systematic review and meta-analyses (PRISMA) (Liberati et al., 2009).

2.1. Search strategy

We conducted a search of PubMed (from 1949), PsycINFO (from 1806), CINAHL (from 1981), and EMBASE (from 1974) from their inception up to August 2013. Search terms were (suicid* OR self-harm* OR self harm* OR self-poison* OR overdose* OR self-injur*) AND (randomiz* OR randomis*). Furthermore, we examined the list of references in the identified studies for further references. We did not distinguish between a suicide attempt and deliberate self-harm or self-injury, because there has been inconsistent use of terminology for suicide attempt and self-harm (Hawton et al., 2012).

We reviewed all titles and abstract, and removed the records that met the exclusion criteria or were duplicated. Full-text articles of possibly eligible studies were reviewed and identified according to inclusion and exclusion criteria by at least two authors independently. Disagreements were discussed with a third author and resolved by consensus.

2.2. Study eligibility

2.2.1. Inclusion criteria

Trials were included if they met the following criteria: all participants had attempted suicidal behavior within 1 month and were admitted to an ED for their suicidal behavior; assessment for eligibility or initial intervention in the trial was performed while the patients were admitted to the ED or a subsequent ward; and an effect of an intervention was examined in a randomized controlled trial and was described in the manuscript.

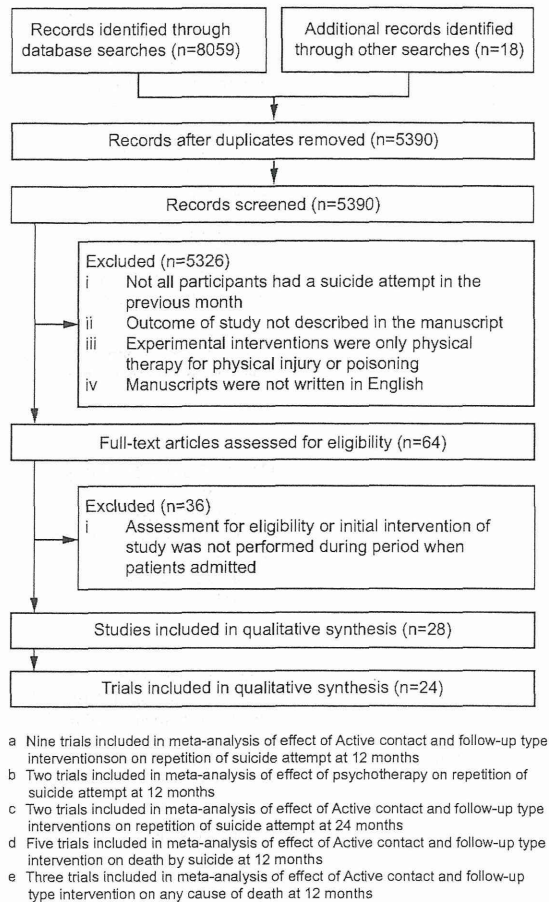


Fig. 1. Identification of studies.

2.2.2. Exclusion criteria

Studies were excluded if they met the following criteria: experimental interventions were only physical therapy for physical injury or poisoning; manuscripts were not written in English; and the main outcome was a subgroup analysis of the trial.

2.3. Data management

We extracted data from the included studies on type of intervention, number of participants, inclusion and exclusion criteria, adherence of participants to interventions, proportion of participants followed up for outcomes, means of establishing suicidal death and/or suicidal behavior if the trial measured these outcomes, and effects of the interventions on repeat suicidal behaviors and death by suicide. We created summary tables of the data. In addition, we summarized the process of development and content of each intervention.

We classified the trials by type of intervention into four groups (Active contact and follow-up, Psychotherapy, Pharmacotherapy, and Miscellaneous). The Active contact and follow-up group consisted of five subgroups (Intensive care plus outreach, Brief intervention and contact, Letter or postcard intervention, Telephone, and Composite of letter/postcard and telephone). The intervention groups were determined by the research members of the study, which included psychiatrists, and psychologists who had experience of working in suicide prevention at EDs.

2.4. Assessment of bias

We also assessed the risk of bias in the included studies according to the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (Cochrane Collaborative, 2011). We judged the quality of the trials from the aspect of sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other potential sources of bias, by at least two authors independently. Disagreements were discussed with a third author and resolved by consensus.

2.5. Statistical analysis

We examined the effects of each intervention group on repeat suicide attempts, deaths by suicide, and any-cause deaths using a meta-analysis. We did not perform a meta-analysis if there was only one trial in an intervention group assessing an outcome at a specific measurement point. We did not analyze any psychometric measures, such as depression, hopelessness, and suicidal ideations, as outcomes because of differences in the measured outcomes and measurement points.

The meta-analysis determined pooled relative risks (RRs) and their 95% confidence intervals (CIs). A fixed-effects model with the Mantel–Haenszel method was used for synthesizing data from trials that examined similar interventions and study populations. Effect estimates were weighted by the inverse of their variance, giving greater weight to a larger sample size. Also, a random-effects model with the DerSimonian–Laird method (DerSimonian and Laird, 1986) was used to produce an overall summary if there was clinical heterogeneity sufficient to suggest that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, and if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects, and the clinical implications of treatment effects differing between trials are discussed.

For assessment of heterogeneity, we used the I^2 and Cochrane Q statistics to examine heterogeneity among the trials in each analysis. We regarded heterogeneity as substantial if I^2 was greater than 30% or there was a low p -value (< 0.10) in the Cochrane Q test for heterogeneity. We investigated publication bias by inspection of funnel plots and by the Egger test.

In trials with three arms, the trials were included in this review as two separate studies; to avoid double counting, the control group data (events and sample) were shared between the two study comparisons (Cochrane Collaborative, 2011). We carried out statistical analysis using the StatsDirect software version 2.8 (StatsDirect Software Inc., Altrincham, UK).

3. Results

3.1. Study inclusion

From 8077 records identified through database and other searches, 5390 articles were retrieved after duplicates were removed. Out of the 5390 articles, we included 24 trials that reported results in 28 publications (Fig. 1) (Aillard et al., 1992; Bannan, 2010; Battaglia et al., 1999; Beautrais et al., 2010; Bertolote et al., 2010; Brown et al., 2005; Carter et al., 2005, 2007, 2013; Cedereke et al., 2002; Crawford et al., 2010; Fleischmann et al., 2008; Ghahramanlou-Holloway et al., 2012; Gibbons et al., 1978; Guthrie et al., 2001; Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Liberman and Eckman, 1981;

Table 1
Intervention.

	Intervention 1	Intervention 2/Comparison intervention	Control(TAU, Placebo)
Active contact and follow-up group (Intensive care plus outreach)			
Allard et al. (1992)	Intensive follow-up with scheduled visits	–	TAU: care by regular personnel of their hospital TAU: outpatient appointment
Van Heeringen et al. (1995)	Home visit by nurse to patients who did not keep outpatient appointment	–	TAU: routine clinical service
van der Sande et al. (1997)	Intensive in-patient and community intervention	–	TAU: referral to a range of different treatment modalities
Morthorst et al. (2012)	Assertive intervention with outreach consultations	–	TAU: the norms prevailing in the respective emergency department
Active contact and follow-up group (Brief intervention and contact)			
Fleischmann et al. (2008), Bertolote et al. (2010)	Brief intervention and contact	–	TAU: assessment and diagnosis by a psychiatrist TAU: assessment and referral to community-based mental health services TAU: follow-up care was not coordinated.
Active contact and follow-up group (Letter or postcard)			
Carter et al. (2005, 2007, 2013)	Postcard sent	–	TAU: assessment by a psychiatrist
Beautrais et al. (2010)	Postcard sent	–	TAU: assessment and referral to community-based mental health services
Hassanian-Moghaddam et al. (2011)	Postcard sent	–	TAU: follow-up care was not coordinated.
Active contact and follow-up group (Telephone)			
Cedereke et al. (2002)	Telephone call at 4 and 8 months	–	TAU: assessment by a psychiatrist and a social counselor and referral to further treatment in general psychiatry TAU: no telephone contact
Vaiva et al. (2006)	Telephone call from psychiatrists at 1 month	Telephone call from psychiatrists at 3 months	–
Active contact and follow-up group (Composite of letter/postcard and telephone)			
Kapur et al. (2013)	Information leaflet, two telephone calls within the first 2 weeks, and a series of 6 letters over a 12-month period	–	TAU: a mental health liaison nursing team to carry out specialist assessments
Psychotherapy group			
Gibbons et al. (1978)	Problem-solving approach	–	TAU: routine service: referral back to a GP, psychiatric referral, or other referral
Liberman and Eckman (1981)	Inpatient treatment with behavioral therapy followed by individual and group therapy plus aftercare at a community mental health center or with private therapists	Inpatient treatment with insight-orientated therapy followed by individual and group therapy plus aftercare at a community mental health center or with private therapists	–
McLeavey et al. (1994)	Problem-solving approach	Brief problem-orientated approach	–
Guthrie et al. (2001)	Psychodynamic interpersonal therapy	–	TAU: an assessment, and if necessary, referral to a psychiatry outpatient, addiction services, or advice to consult their own GPs
Raj et al. (2001)	Cognitive behavioral method to enhance compliance	Routine medical treatment plus provision of therapist contact information, and contact by letters twice	–
Brown et al. (2005), Ghahramanlou-Holloway et al. (2012)	Cognitive therapy	–	TAU: care from clinicians in the community and referral services from the study case manager, and contact from case manager
Bannan (2010)	Problem-solving approach	–	TAU: standard individual therapy in the outpatients or day hospital TAU: Standard psychosocial assessment
Ougrin et al. (2011)	Therapeutic assessment: a brief intervention based on cognitive analytic therapy	–	–
Wei et al. (2013)	Cognitive therapy	Telephone intervention	TAU: All patients in the three groups received necessary psychotropic medication if necessary
Pharmacotherapy group			
Battaglia et al. (1999)	Low dose of depot fluphenazine	Ultra-low dose of depot fluphenazine	–
Miscellaneous group			
Torchorst et al. (1987)	Continuity of care: therapy with the same therapist who assessed the patient in hospital after a suicide attempt	Change of care: therapy with a different therapist	–

Table 1 (continued)

	Intervention 1	Intervention 2/Comparison intervention	Control(TAU, Placebo)
Waterhouse and Platt (1990)	Admission to a general hospital, and advice to contact their GP after discharge from hospital, if needed	Discharge home from the casualty department with advice to contact their GP, if needed	
Crawford et al. (2010)	Provision of an appointment card with alcohol nurse specialist and a health information leaflet	Provision of a health information leaflet	-

Abbreviations: TAU, treatment as usual.

McLeavey et al., 1994; Morthorst et al., 2012; Ougrin et al., 2011; Raj et al., 2001; Torhorst et al., 1987; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995; Waterhouse and Platt, 1990; Wei et al., 2013).

3.2. Characteristics of included trials

We classified the 24 trials into four categories: 11 trials in the Active contact and follow-up group, nine in the Psychotherapy group, one in the Pharmacotherapy group, and three in the Miscellaneous group (Table 1).

3.2.1. Active contact and follow-up group

We sub-classified the 11 trials into five subgroups: four trials in Intensive care plus outreach, one trial in Brief intervention and contact, three in Letter/postcard, two in Telephone, and one in a Composite of letter/postcard and telephone subgroup.

3.2.1.1. Intensive care plus outreach. Morthorst et al. (2012) examined the effects of contact with suicide attempters at the ED followed by 8–20 outreaches for 6 months by a specialized nurse on repeat suicide attempts. Their intervention was based on one developed and performed by a specialized prevention team for over 20 years in Norway on suicide attempters in the ED without psychosis (Hvid et al., 2011; Johannessen et al., 2011). In another study, Van Heeringen et al. (1995) examined the effect of case-management, with two home visits by a community nurse to increase adherence to care. The intervention was developed using a previous intervention developed by Moller (1989) as a model, which involved continuity of care.

Around the same time, van der Sande et al. (1997) performed a trial to examine effects of an intervention based on a problem-solving approach, which had been developed by Hawton and Catalan (1987) as a model. The intervention was performed by community psychiatric nurses who were assigned to establish a therapeutic relationship with each patient during hospitalization, and focused on helping the patient to overcome the current crisis and on establishing improvements in their ability to cope with future problems.

In an earlier report, Allard et al. (1992) showed no clear effect of an intervention, including at least one home visit by social workers on repeat suicide attempts.

3.2.1.2. Brief intervention and contact. Motto (1976) and Motto and Bostrom (2001) reported a reduction in suicide attempts in psychiatric patients by long-term contact. In another study, De Leo et al. (1995, 2002) reported a reduction in suicidal deaths among elderly people contacted by telephone. Based on these findings, the World Health Organization performed the SUPRE-MISS trial, which was a long-term follow-up with brief contact intervention (Bertolote et al., 2010; Fleischmann et al., 2008).

3.2.1.3. Letter/postcard. Carter et al. (2005, 2007, 2013) investigated the effect of sending a series of eight postcards after

discharge to patients who were admitted to EDs with poisoning self-injury. The intervention was developed using a previous intervention as a model, which showed fewer suicide deaths among a psychiatric hospital inpatient population (Motto, 1976; Motto and Bostrom, 2001). Carter et al. reported that postcard intervention reduced repeat poisoning after 1 year (Carter et al., 2005), 2 years (Carter et al., 2007), and 5 years (Carter et al., 2013). They also reproduced similar results among self-poisoning patients admitted to a poisoning center in a trial performed in Iran (Hassanian-Moghaddam et al., 2011). However, another trial of a similar intervention in self-poisoning patients and suicide attempters with other self-injuries did not show a reduction in repeat suicide attempts after adjusting for baseline characteristics (Beautrais et al., 2010).

3.2.1.4. Telephone. Cedereke et al. (2002) developed a new intervention, which consisted of two telephone calls to suicide attempters discharged from EDs. The intervention was based on a report that long-term contact reduced suicide deaths in psychiatric in-patients (Motto, 1976; Motto and Bostrom, 2001). Vaiva et al. (2006) referred to the paper by Cedereke et al. (2002), and compared suicidal attempts between two interventions; one was a telephone call 1 month after discharge from the ED, and the other was a telephone call 3 months after discharge.

3.2.1.5. Composite of letter/postcard and telephone intervention. Recently, Kapur et al. (2013) developed a composite of contact-type interventions. This consisted of an information leaflet listing local and national sources of help, two telephone calls within the first 2 weeks, and then a series of letters over a 12-month period (at 1, 2, 4, 6, 8, and 12 months). The intervention was developed using qualitative interviews and focus groups with service users and providers (Kapur et al., 2010). Contrary to the preventive effect of postcards shown in studies by Carter et al. (2005, 2007, 2013), the trial showed increased rates of repeat suicide in the intervention group compared with the established treatment control group.

3.2.2. Psychotherapy group

Several different approaches were reported, including cognitive therapy (Brown et al., 2005; Ghahramanlou-Holloway et al., 2012; Wei et al., 2013), problem-solving approach (Bannan, 2010; Gibbons et al., 1978; McLeavey et al., 1994), psychodynamic interpersonal therapy (Guthrie et al., 2001), cognitive analytic therapy (Ougrin et al., 2011), insight-oriented therapy and behavioral therapy (Lieberman and Eckman, 1981), and cognitive behavioral method to enhance compliance (Raj et al., 2001). Some trials focused only on changes in psychometric outcomes and did not examine suicidal deaths and repeat suicide attempts (Ougrin et al., 2011; Raj et al., 2001; Waterhouse and Platt, 1990).

3.2.3. Pharmacotherapy group

A study examined differences in rates of repeat suicide attempts between patients without schizophrenia who had repeated suicide attempts and were treated with very low-dose

fluphenazine or low-dose fluphenazine (Battaglia et al., 1999). Although rates of self-harm behaviors per month were reduced in both groups, there was no clear difference between the groups.

3.2.4. Miscellaneous group

We classified three trials into the “Miscellaneous group”. One of the trials compared adherence to treatment between referral to a specialized suicide prevention center and continuous therapeutic contact with the original hospital therapist in an outpatient setting (Torhorst et al., 1987). The comparison was inspired by a finding of low adherence of suicide attempters to intervention (Kurx and Moller, 1984). The group of patients who received continuous therapeutic contact showed a lower rate of further suicidal behavior measured as a secondary outcome. Another study examined the effects of transfer to a general hospital compared with discharge home on the suicide repetition rate (Waterhouse and Platt, 1990). However, there were no differences in any of the measured outcomes. The third study examined the effect of referral for brief intervention for alcohol misuse on repetition of deliberate self-harm among patients with alcohol misuse presenting to an ED for deliberate self-harm (Crawford et al., 2010). Referral for brief intervention for alcohol misuse may not influence the likelihood of repeat self-harm.

3.3. Risk of bias

We assessed the risk of bias in the included studies according to the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Collaborative, 2011). The results are shown in Table 2.

Among nine trials (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) in the Active contact and follow-up group at 12 months ($n=5319$), three (Hassanian-Moghaddam et al., 2011; Morthorst et al., 2012; van der Sande et al., 1997), two (Vaiva et al., 2006; Van Heeringen et al., 1995), seven (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Kapur et al., 2013; Morthorst et al., 2012; Vaiva et al., 2006; Van Heeringen et al., 1995), and seven trials (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Kapur et al., 2013; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) were assessed as having a high risk of bias related to blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources, respectively. Among two (Allard et al., 1992; Carter et al., 2007) trials in the Active contact and follow-up at 24 months ($n=925$) for a repeat suicide attempt, one (Allard et al., 1992), two (Allard et al., 1992; Carter et al., 2007),

Table 2
Risk of bias.

	Random sequence generation	Allocation sequence concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other potential sources of bias
Active contact and follow-up group (Intensive care plus outreach)							
Allard et al. (1992)	Unclear	Low	Unclear	Unclear	High	High	High
Van Heeringen et al. (1995)	Low	Unclear	Unclear	Unclear	High	High	High
van der Sande et al. (1997)	Low	Low	Unclear	High	Unclear	Low	High
Morthorst et al. (2012)	Low	Low	Unclear	High	Low	High	Low
Active contact and follow-up group (Brief intervention and contact)							
Fleischmann et al. (2008), Bertolote et al. (2010)	Low	Low	Unclear	Unclear	High	Low	High
Active contact and follow-up group (Letter or postcard)							
Carter et al. (2005, 2007, 2013)	Low	Low	Unclear	Low	Unclear	High	High
Beautrais et al. (2010)	Low	Low	Unclear	Low	Low	High	High
Hassanian-Moghaddam et al. (2011)	Low	Low	Low	High	Low	Low	Low
Active contact and follow-up group (Telephone)							
Cedereke et al. (2002)	Low	Low	Low	Low	Low	High	High
Vaiva et al. (2006)	Low	Low	Unclear	Low	High	High	High
Active contact and follow-up group (Composite of letter/postcard and telephone)							
Kapur et al. (2013)	Low	Low	Unclear	Low	Low	High	High
Psychotherapy group							
Gibbons et al. (1978)	High	High	Unclear	Low	High	High	Unclear
Lieberman and Eckman (1981)	Unclear	Unclear	Unclear	Unclear	Low	High	High
McLeavey et al. (1994)	Unclear	Unclear	Unclear	Low	Unclear	High	High
Guthrie et al. (2001)	Low	Unclear	Unclear	Low	Low	Low	High
Raj et al. (2001)	High	High	Unclear	Unclear	Unclear	High	High
Brown et al. (2005), Ghahramanlou-Holloway et al. (2012)	Low	Low	High	High	Low	Low	High
Bannan (2010)	Low	Low	High	Low	Unclear	High	High
Ougrin et al. (2011)	Low	Low	High	Low	High	Low	High
Wei et al. (2013)	Low	Unclear	Unclear	Unclear	High	High	High
Pharmacotherapy group							
Battaglia et al. (1999)	Unclear	Unclear	High	Unclear	High	High	High
Miscellaneous group							
Torhorst et al. (1987)	Unclear	Unclear	Unclear	Unclear	High	High	High
Waterhouse and Platt (1990)	Unclear	Low	Unclear	High	Low	High	Unclear
Crawford et al. (2010)	Low	Low	Unclear	Unclear	Low	Low	High

Abbreviations: Low, low risk of bias; plausible bias unlikely to seriously alter the results; Unclear, unclear risk of bias; plausible bias that raises some doubt about the results; High, high risk of bias; plausible bias that seriously weakens confidence in the results.

and two trials (Allard et al., 1992; Carter et al., 2007) were assessed as having a high risk of bias related to incomplete outcome data, selective outcome reporting, and other potential sources, respectively. Among five trials (Cedereke et al., 2002; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) in the Active contact and follow-up group at 12 months ($n=1854$) for suicidal death, two (Morthorst et al., 2012; van der Sande et al., 1997), two (Vaiva et al., 2006; Van Heeringen et al., 1995) four (Cedereke et al., 2002; Morthorst et al., 2012; Vaiva et al., 2006; Van Heeringen et al., 1995), and four trials (Cedereke et al., 2002; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) were assessed as having a high risk of bias related to blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources, respectively. Each or both of two Psychotherapy trials (Gibbons et al., 1978; Wei et al., 2013) for a repeat suicide attempt at 12 months ($n=559$) were assessed as having a high risk of bias related to random sequence generation, allocation sequence concealment, incomplete outcome data, selective outcome reporting, and other potential source.

The total number of participants in the target intervention group in 24 trials was 4169, and the median (range) of the sample size among the 24 trials was 72 (9–1150) (Supplementary Table 1). Ten trials (Beautrais et al., 2010; Bertolote et al., 2010; Carter et al., 2005, 2007, 2013; Cedereke et al., 2002; Fleischmann et al., 2008; Gibbons et al., 1978; Hassanian-Moghaddam et al., 2011; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) had more than 100 participants in the intervention group. All trials classified as psychotherapy (Bannan, 2010; Brown et al., 2005; Ghahramanlou-Holloway et al., 2012; Guthrie et al., 2001; Liberman and Eckman, 1981; McLeavey et al., 1994; Ougrin et al., 2011; Raj et al., 2001; Wei et al., 2013), except one by Gibbons et al. (1978), the one classified as pharmacotherapy (Battaglia et al., 1999) and the three classified as miscellaneous group (Crawford et al., 2010; Torhorst et al., 1987; Waterhouse and Platt, 1990), had less than 100 participants in the intervention group.

Several trials excluded patients with a high risk of suicide (Allard et al., 1992; Gibbons et al., 1978; McLeavey et al., 1994; Ougrin et al., 2011), and other trials excluded patients with psychosis (Bannan, 2010; Battaglia et al., 1999; Gibbons et al., 1978; Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Liberman and Eckman, 1981; McLeavey et al., 1994; Morthorst et al., 2012; Raj et al., 2001; Torhorst et al., 1987). Some studies examined the effect of

interventions in patients with repeat suicide attempts and multiple deliberate self-harm episodes (Bannan, 2010; Battaglia et al., 1999; Liberman and Eckman, 1981). A number of studies did not mention the proportion of participants who adhered to their intervention (Supplementary Table 2). Among the remaining studies showing information about adherence of participants to the intervention, the proportion was generally low.

Several studies set a repeat suicide attempt (Brown et al., 2005; Carter et al., 2005, 2007, 2013; Crawford et al., 2010; Ghahramanlou-Holloway et al., 2012; Hassanian-Moghaddam et al., 2011; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997) and/or death by suicide (Bertolote et al., 2010; Fleischmann et al., 2008; Morthorst et al., 2012; Vaiva et al., 2006) as one of their primary outcomes (Supplementary Table 3). However, some trials reporting repeat suicide attempt and/or death by suicide did not clearly state which outcome was the primary outcome (Allard et al., 1992; Battaglia et al., 1999; Beautrais et al., 2010; Cedereke et al., 2002; Gibbons et al., 1978; Guthrie et al., 2001; Kapur et al., 2013; Liberman and Eckman, 1981; McLeavey et al., 1994; Van Heeringen et al., 1995; Wei et al., 2013). Some reported psychometric and other outcomes as their primary outcome, and suicide attempts and/or death by suicide were not measured (Ougrin et al., 2011; Raj et al., 2001; Waterhouse and Platt, 1990).

Among the trials examining the effect of the interventions on repetition of suicidal behavior as the outcome, the methods of measuring the repeat suicide attempt were different as shown in Supplementary Table 3.

No publication bias was detected by the funnel plot or the Egger test.

3.4. Outcome findings

3.4.1. Repeat suicidal behavior

We performed a meta-analysis to examine the effect of each intervention group on repeat suicide within 12 months. Among the 24 trials, 11 reported the effects of interventions on a repeat suicide attempt within 12 months (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Gibbons et al., 1978; Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995; Wei et al., 2013).

The results of a meta-analysis of nine trials ($n=5319$) of Active contact and follow-up group (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Hassanian-Moghaddam et al., 2011;

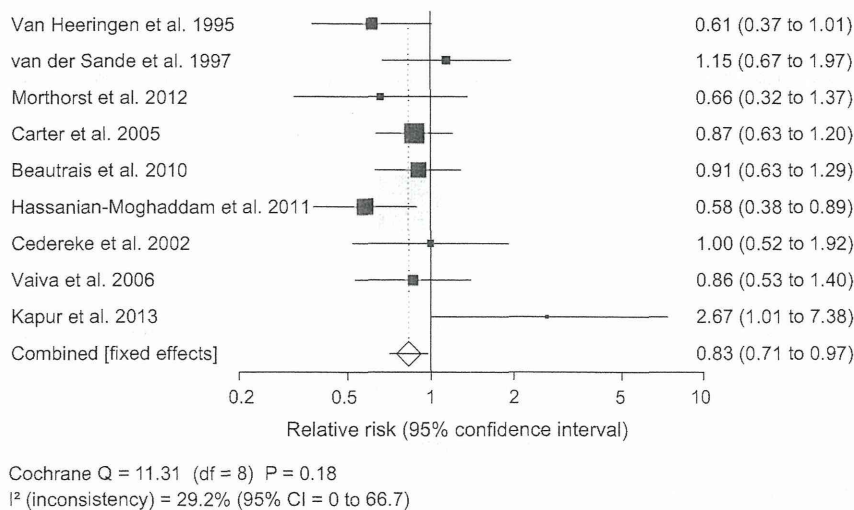


Fig. 2. Repeat suicide attempt within 12 months in Active contact and follow-up intervention studies.

Kapur et al., 2013; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995) are shown in Fig. 2. There was a statistically significant effect on prevention of a repeat suicide attempt (RR: 0.83; 95% CI: 0.71–0.97). Using the results of the medical chart review instead of the results of the telephone interview in the trial by Morthorst et al. (2012), the pooled RR (95% CI) increased to 0.90 (0.73–1.12), with no statistical significance. The pooled RR at 12 months of three trials ($n=1033$) of Intensive care plus outreach of Active contact and follow-up group (Morthorst et al., 2012; van der Sande et al., 1997; Van Heeringen et al., 1995) was 0.79 (95% CI: 0.52–1.19) (Cochrane $Q=3.00$, $p=0.22$; $I^2=33.1\%$, 95% CI=0–80.9). The pooled RR of six trials in the Letter/postcard and telephone intervention of Active contact and follow-up group ($n=4286$) (Beautrais et al., 2010; Carter et al., 2005; Cedereke et al., 2002; Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Vaiva et al., 2006) was 0.87 (95% CI: 0.68–1.12) (Cochrane $Q=8.13$, $p=0.15$; $I^2=38.5\%$, 95% CI=0–74.5).

The RR at 12 months of two psychotherapy trials ($n=559$) (Gibbons et al., 1978; Wei et al., 2013) was 0.86 (95% CI=0.54–1.37) as shown in Fig. 3.

Regarding repeat suicide attempts within 18 months, each group had no or only one trial.

For repeat suicide attempts within 24 months, there were only two trials ($n=925$), both in the Active contact and follow-up group (Allard et al., 1992; Carter et al., 2007) (Fig. 4) and none in the other groups (Table 3). The pooled RR was 0.97 (95% CI: 0.76–1.22) as shown in Fig. 4.

3.4.2. Suicidal death

In the Active contact and follow-up intervention group, there were five trials ($n=1854$) reporting the outcome of death by suicide within 12 months (Cedereke et al., 2002; Morthorst et al., 2012; Vaiva et al., 2006; van der Sande et al., 1997; Van Heeringen et al., 1995). The pooled RR and the 95% CI are shown in Fig. 5 (RR: 0.83; 95% CI: 0.36–1.90).

3.4.3. Outcome: any cause of death

Three trials ($n=2609$) reported outcomes of any cause of death within 12 months in the Active contact and follow-up intervention group (Hassanian-Moghaddam et al., 2011; Kapur et al., 2013; Morthorst et al., 2012). The pooled RR and 95% CI are shown in Fig. 6 (RR: 2.97; 95% CI: 0.89–9.90).

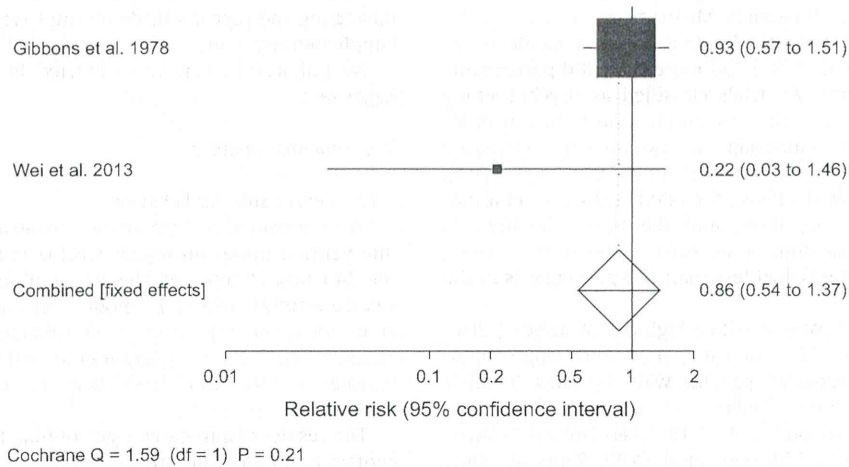


Fig. 3. Repeat suicide attempt within 12 months in Psychotherapy intervention studies.

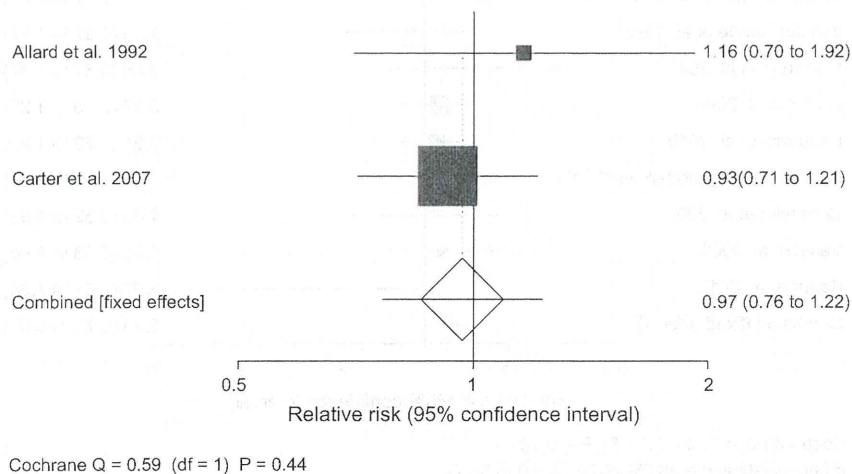


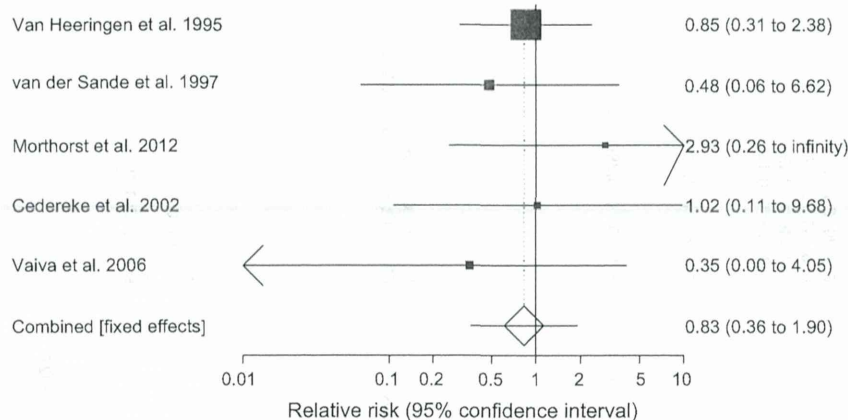
Fig. 4. Repeat suicide attempt within 24 months in Active contact and follow-up intervention studies.

Table 3
Results.

	Re-attempt		Death	
	No. of patients with re-attempt/No. of patients used in the analysis in each group	No. of re-attempts/No. of patients used in the analysis in each group	No. of any-cause deaths/No. of patients in the analysis in each group	No. of suicidal deaths/No. of patients used in the analysis in each group
Active contact and follow-up group (Intensive care plus outreach)				
Allard et al. (1992)	E: 22/63; C: 19/63	E: 60/63; C: 54/63	–	E: 3/76; C: 1/74
Van Heeringen et al. (1995)	E: 21/196; C: 34/195	–	15 died in both groups	E: 6/196; C: 7/195
van der Sande et al. (1997)	E: 24/140; C: 20/134	E: 32/140; C: 31/134	–	E: 1/140; C: 2/134
Morthorst et al. (2012)	E: 20/123; C: 13/120 (medical recorded) E: 11/95; C: 13/74 (self-reported)	–	E: 2/123; C: 1/120	E: 1/123; C: 0/120
Active contact and follow-up group (Brief intervention and contact)				
Fleischmann et al. (2008), Bertolote et al. (2010)	E: 66/863; C: 60/800	–	E: 11/872; C: 22/827	E: 2/872; C: 18/827
Active contact and follow-up group (Letter or postcard)				
Carter et al. (2005, 2007, 2013)	E: 57/378; C: 68/394 in 12 months	E: 101/378; C: 192/394 in 12 months	E: 22/378; C: 22/394 in 60 mo	E: 5/378; C: 6/394 in 60 mo
	E: 80/378; C: 90/394 in 24 months	E: 145/378; C: 310/394 in 24 months	–	–
	E: 94/378; C: 107/394 in 60 months	E: 252/378; C: 484/394 in 60 months	–	–
Beautrais et al. (2010)	E: 39/153; C: 49/174	E: 87/153; C: 136/174	–	–
Hassamian-Moghaddam et al. (2011)	E: 31/1043; C: 55/1070	E: 34/1043; C: 58/1070	E: 7/1150; C: 2/1150	–
Active contact and follow-up group (Telephone)				
Cedereke et al. (2002)	E: 14/83 vs. C: 15/89	E: 26/83 vs. C: 27/89	–	E: 1/107; C: 1/109
Vaiva et al. (2006)	E1: 24/147; E2: 20/146; C: 59/312	–	6 died in three groups	E1: 0/147; E2: 1/146; C: 2/312
Active contact and follow-up group (Composite of letter/postcard and telephone)				
Kapur et al. (2013)	E: 11/33; C: 4/32	E: 41/33; C: 7/32	E: 1/33; C: 0/32	–
Psychotherapy group				
Gibbons et al. (1978)	E: 27/200; C: 29/200	–	–	–
Liberman and Eckman (1981)	E1: 3/12; E2: 2/12	E1: 5/12; E2: 6/12	–	–
McLeavey et al. (1994)	^a E1: 2/19; E2: 5/20	–	–	–
Guthrie et al. (2001)	E: 5/58; C: 17/61	–	–	E: 0/58; C: 0/61
Raj et al. (2001)	–	–	–	–
Brown et al. (2005), Ghahramanlou-Holloway et al. (2012)	E: 13/45; C: 23/40	–	E: 1/45; C: 3/40	E: 0/45; C: 1/40
Bannan (2010)	E: 0/9; C: 0/9	–	–	–
Ougrin et al. (2011)	–	–	–	–
Wei et al. (2013)	E1: 1/25; E2: 1/36; C: 5/27	–	E1: 1/25; E2: 0/36; C: 0/27	–
Pharmacotherapy group				
Battaglia et al. (1999)	The numbers of patients with re-attempt were not shown ($p=0.15$ in change of numbers of "serious" self-harm/month between E1 and E2)	–	–	–
Miscellaneous group				
Torhorst et al. (1987)	E1: 12/65; E2: 4/68	–	–	–
Waterhouse and Platt (1990)	–	–	–	–
Crawford et al. (2010)	E1: 7/51; E2: 11/52	–	E1: 1/51; E2: 0/52	–

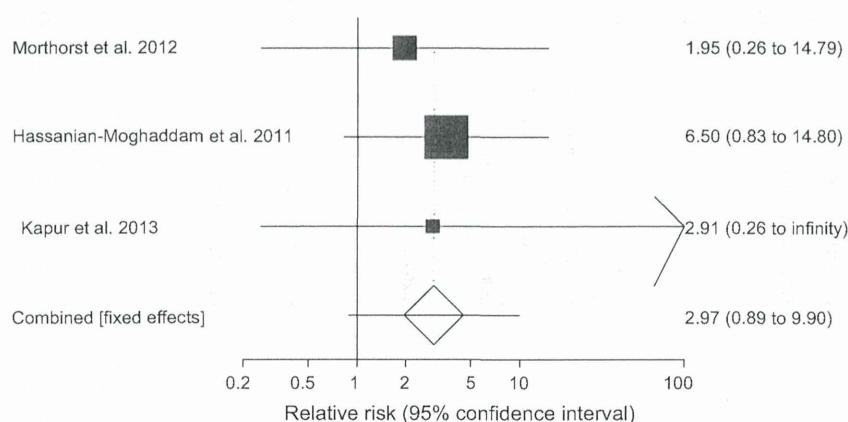
Abbreviations: E, experimental intervention group; C, control group.

^a Five patients who dropped out from treatment were not assessed.



Cochrane Q = 1.10 (df = 4) P = 0.89
 I^2 (inconsistency) = 0% (95% CI = 0 to 64.1)

Fig. 5. Suicide deaths within 12 months in Active contact and follow-up intervention studies.



Cochrane Q = 2.97 (df = 2) P = 0.92
 I^2 (inconsistency) = 0% (95% CI = 0 to 72.9)

Fig. 6. Any-cause deaths within 12 months in Active contact and follow-up intervention studies.

4. Discussion

4.1. Summary of results of the meta-analysis

Twenty-four trials were identified and classified into four intervention groups (Active contact and follow-up, Psychotherapy, Pharmacotherapy, and Miscellaneous). Our meta-analysis showed that active contact and follow-up type interventions were effective in preventing a repeat suicide within 12 months in patients admitted to EDs for a suicide attempt. However, the long-term effect at 24 months was not confirmed. Also, the effects of the interventions in preventing death by suicide has not been confirmed yet, because the number of trials assessing suicidal deaths was small, and the sample size of each trial was too small to detect significant differences in deaths by suicide.

The effects of the other interventions in preventing a repetition of suicidal behavior remain unclear. In some trials (Allard et al., 1992; Battaglia et al., 1999; Brown et al., 2005; Crawford et al., 2010; Ghahramanlou-Holloway et al., 2012; Gibbons et al., 1978; Guthrie et al., 2001; Torhorst et al., 1987; Wei et al., 2013), the proportion of adherence to interventions was relatively low. In addition, some trials examined only psychometric outcomes, and not suicidal behavior. The proportion of follow-up of outcomes in some trials (Brown et al., 2005; Cedereke et al., 2002;

Ghahramanlou-Holloway et al., 2012; Van Heeringen et al., 1995; Wei et al., 2013) was also low.

4.2. Comparison with other systematic reviews

Previously, Luxton et al. performed a systematic review to examine the effect of follow-up interventions on suicidal behavior in patients discharged from inpatient psychiatry departments and EDs (Luxton et al., 2013). However, they did not perform a meta-analysis. They reported that repeated follow-up contact reduced suicidal behavior, based on the finding that three of 11 trials showed a statistically significant reduction in repeat suicidal attempts, and two studies reported a reduction in suicidal deaths. Our findings are consistent with their report. Therefore, our present study confirmed and extended their initial findings with meta-analysis.

Several systematic reviews have previously been published, although the participants were not limited to patients admitted to the ED after suicidal injury. Hawton et al. (1998, 2009) performed a systematic review to examine the effects of psychosocial and pharmacological interventions on deliberate self-harm. However, the number of trials was too small at that time, and the review concluded that there remains considerable uncertainty regarding the outcome of the interventions. Crawford et al. (2007)

performed another systematic review of psychosocial interventions following self-harm. The meta-analysis included 18 trials with various intervention types and suggested that psychosocial interventions had no marked effect on suicide deaths. O'Connor et al. (2013) showed a significant effect of psychotherapy and a positive trend of the effect of enhanced usual care on suicide attempts in primary care settings (pooled RR: 0.86; 95% CI: 0.56–0.83 in 11 trials). Therefore, our present study confirms the beneficial effect of interventions at least for patients admitted to the ED with suicidal injury.

4.3. Strengths and limitations of study

This is the first systematic review and meta-analysis assessing the effects of interventions in patients admitted to the ED for injury caused by their suicidal behavior. The results of the meta-analysis suggest that interventions of active contact and follow-up reduce the risk of a repeat suicide attempt at 12 months. The findings may have implications for future clinical policy-making to prevent repeat suicidal behavior in patients admitted to the ED for a suicide attempt.

There are several limitations of this review. We classified the type of interventions for convenience into Active contact and follow-up, Psychotherapy, Pharmacotherapy, and Miscellaneous groups, but many of the trials combined several interventions. Although the I^2 and Cochrane Q statistics were smaller than 30% and more than 0.10, respectively, in most of the meta-analyses, caution is needed regarding the heterogeneity of the effects and the interpretation of the results. In addition, for the outcome of suicidal deaths, the statistical power was too weak to conclude that there was a beneficial effect of intervention because the number of deaths by suicide was very low even in the high-risk ED population.

4.4. Implication for research

Although our present systematic review showed the effectiveness of active contact and follow-up interventions to reduce the risk of a repeat attempt at 12 months, a large, quality, randomized controlled trial is needed to confirm our findings. In addition, a long-term effect of the intervention has not been confirmed in this study. When a long-term effect is not demonstrated, further studies are required to develop a novel intervention to reduce the long-term risk of a repeat suicide attempt.

The proportion of follow-up interviews with participants was relatively low compared with the proportion of medical records used for follow-up. A previous study reported paradoxical results between results obtained from medical record and those from self-report (Morthorst et al., 2012). Given that the validity of each assessment measure may be different, a valid and consistent assessment measure is needed for future trials.

Many trials did not measure and/or report adherence to intervention, even though some trials hypothesized that increasing adherence to intervention is a key process in preventing suicide. There may be room for improvement in increasing adherence to intervention to increase the effectiveness of intervention in preventing suicidal behavior and death by suicide.

In this study, the effects of interventions on death by suicide were unclear, because the number of trials assessing suicidal deaths was small. More studies are needed to determine the effect of interventions on suicidal deaths.

4.5. Implication for practice

Interventions of active contact and follow-up are recommended to reduce the risk of a repeat suicide attempt in patients

admitted to the ED for a suicide attempt at 12 months. It is already known that a majority of suicide attempters suffer from severe psychiatric disorders including mood disorders (Beautrais et al., 1996; Haw et al., 2001; Hawton et al., 2003; Kawashima et al., 2014; Rihmer et al., 2009; Suominen et al., 1996; Yamada et al., 2007). However, suicide attempters are often discharged from EDs without undergoing a psychiatric assessment, despite their risk of suicide (Hickey et al., 2001; Olfson et al., 2013). In EDs, it can be difficult to assess patients who often leave without a psychiatric evaluation or who are admitted to the ED on evenings and weekends when psychiatric staff availability may be limited (Bennewith et al., 2004; Hickey et al., 2001). Even though patients may be referred for outpatient treatment follow-up after ED discharge, only 25–50% actually attend outpatient appointments within 1 month of the suicide attempt (Van Heeringen et al., 1995). Implementation of procedures for assessment of patients and for monitoring adherence to interventions would be expected.

5. Conclusion

This meta-analysis suggests that interventions of active contact and follow-up may reduce the risk of a repeat suicide attempt at 12 months in patients admitted to the ED with suicidal injury. However, the long-term effects in preventing further suicidal behavior and death by suicide were not confirmed. Therefore, large, randomized, controlled trials with better quality and comparable outcome measures are needed to confirm the effectiveness of interventions.

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Conflict of interest

Dr. Inagaki reports grants from the Ministry of Health, Labour and Welfare, personal fees from Pfizer Japan Inc., personal fees from Mochida Pharmaceutical Co., Ltd., personal fees from Nippon Hyoron Sha Co., Ltd., personal fees from Nanzando Co., Ltd., personal fees from Seiwa Shoten Co., Ltd., personal fees from Igaku-shoin Ltd., and personal fees from Technomics, Inc., outside the submitted work. Dr. Kawanishi reports grants from The Ministry of Health, Labour and Welfare, Japan, grants from The Ministry of Education, Culture, Sports, Science and Technology, Japan, grants from The Japan Science and Technology Agency, personal fees from Meiji Seika Pharma Co., Ltd., personal fees from GlaxoSmithKline K.K., and personal fees from Pfizer K.K., outside the submitted work. Dr. Ikeshita reports personal fees from Mochida Pharmaceutical Co., Ltd., outside the submitted work. Dr. Yamada reports grants from The Ministry of Health, Labour and Welfare, Japan, during the conduct of the study; grants from The Ministry of Education, Culture, Sports, Science and Technology, Japan, grants from The Japan Science and Technology Agency, grants from National Center of Neurology and Psychiatry, personal fees from Meiji Seika Pharma Co., Ltd., personal fees from MSD K.K., personal fees from Asahi Kasei Pharma Corporation, personal fees from Seishin Shobo, personal fees from Seiwa Shoten Co., Ltd., personal fees from Igaku-shoin Ltd., personal fees from Chogai Igakusha, and personal fees from Sentan Igakusha, outside the submitted work. No other authors report potential conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.jad.2014.12.048>.