Assertive case management versus enhanced usual care for people with mental health problems who had attempted suicide and were admitted to hospital emergency departments in Japan (ACTION-J): a multicentre, randomised controlled trial

Chiaki Kawanishi, Tohru Aruga, Naoki Ishizuka, Naohiro Yonemoto, Kotaro Otsuka, Yoshito Kamijo, Yoshiro Okubo, Katsumi Ikeshita, Akio Sakai, Hitoshi Miyaoka, Yoshie Hitomi, Akihiro Iwakuma, Toshihiko Kinoshita, Jotaro Akiyoshi, Naoshi Horikawa, Hideto Hirotsune, Nobuaki Eto, Nakao Iwata, Mototsugu Kohno, Akira Iwanami, Masaru Mimura, Takashi Asada, Yoshio Hirayasu, for the ACTION-J Group*

Summary

Background Non-fatal suicide attempt is the most important risk factor for later suicide. Emergency department visits for attempted suicide are increasingly recognised as opportunities for intervention. However, no strong evidence exists that any intervention is effective at preventing repeated suicide attempts. We aimed to investigate whether assertive case management can reduce repetition of suicide attempts in people with mental health problems who had attempted suicide and were admitted to emergency departments.

Methods In this multicentre, randomised controlled trial in 17 hospital emergency departments in Japan, we randomly assigned people aged 20 years and older with mental health problems who had attempted suicide to receive either assertive case management (based on psychiatric diagnoses, social risks, and needs of the patients) or enhanced usual care (control), using an internet-based randomisation system. Interventions were provided until the end of the follow-up period (ie, at least 18 months and up to 5 years). Outcome assessors were masked to group allocation, but patients and case managers who provided the interventions were not. The primary outcome was the incidence of first recurrent suicidal behaviour (attempted suicide or completed suicide); secondary outcomes included completed suicide and all-cause mortality. This study is registered at ClinicalTrials.gov (NCT00736918) and UMIN-CTR (C000000444).

Findings Between July 1, 2006, and Dec 31, 2009, 914 eligible participants were randomly assigned, 460 to the assertive case management group and 456 to the enhanced usual care group. We noted no significant difference in incidence of first recurrent suicidal behaviour between the assertive case management group and the enhanced usual care group over the full study period (log-rank p=0·258). Because the proportional hazards assumption did not hold, we did ad-hoc analyses for cumulative incidence of the primary outcome at months 1, 3, 6, 12, and 18 after randomisation, adjusting for multiplicity with the Bonferroni method. Assertive case management significantly reduced the incidence of first recurrent suicidal behaviour up to the 6-month timepoint (6-month risk ratio 0·50, 95% CI 0·32–0·80; p=0·003), but not at the later timepoints. Prespecified subgroup analyses showed that the intervention had a greater effect in women (up to 18 months), and in participants younger than 40 years and those with a history of previous suicide attempts (up to 6 months). We did not identify any differences between the intervention and control groups for completed suicide (27 [6%] of 460 *vs* 30 [7%] of 454, log-rank p=0·660) or all-cause mortality (46 [10%] of 460 *vs* 42 [9%] of 454, log-rank p=0·698).

Interpretation Our results suggest that assertive case management is feasible in real-world clinical settings. Although it was not effective at reducing the incidence of repetition of suicide attempts in the long term, the results of our ad-hoc analyses suggested that it was effective for up to 6 months. This finding should be investigated in future research.

Funding The Ministry of Health, Labour, and Welfare of Japan.

Lancet Psychiatry 2014; 1: 193–201

See Comment page 165

*Members listed in appendix

Health Management and Promotion Center (C Kawanishi MD) and Department of Psychiatry (Y Hirayasu MD), Yokohama City University Graduate School of Medicine, Yokohama, Japan; Department of Emergency and Critical Care Medicine (T Aruga MD) and Department of Psychiatry (A Iwanami MD), Showa University School of Medicine, Tokyo, Japan; Center for Clinical Sciences, National Center for Global Health and Medicine, Tokyo, Japan (N Ishizuka PhD); Translational Medical Center, National Center of Neurology and Psychiatry, Tokyo, Japan (N Yonemoto MPH); Department of Neuropsychiatry, Iwate Medical University, Morioka, Japan (K Otsuka MD, A Sakai MD); Department of Emergency and Critical Care Medicine (Y Kamijo MD) and Department of Psychiatry (H Miyaoka MD), Kitasato University School of Medicine, Sagamihara, Japan; Department of Neuropsychiatry, Nippon Medical School, Tokyo, Japan (Y Okubo MD); Department of Psychiatry, Nara Medical University, Kashihara, Japan (K Ikeshita MD); Department of Neuropsychiatry, Kinki University Faculty of Medicine, Osakasayama, Japan (Y Hitomi MD); Department of Psychiatry, Mito Medical Center, Mito, Japan (A Iwakuma MD); Department of Neuropsychiatry, Kansai Medical University, Hirakata, Japan (T Kinoshita MD);

Introduction

Non-fatal suicide attempt is the most potent predictor of later suicide.[1–3] Hospital admissions because of attempted suicide and self-inflicted injury have been increasing worldwide.[3,4] The average number of admissions to emergency departments for attempted suicide and self-inflicted injury per year in the USA more than doubled from about 244000 in 1993–96 to 538000 in 2005–08.[5] In the UK, roughly 220000 patients are admitted to hospital for self-harming annually.[3] Emergency department admission for attempted suicide is therefore increasingly recognised as an opportunity for medical personnel to intervene to prevent future suicide attempts.[6]

Several randomised controlled trials have been done to assess the effectiveness of contact interventions (letters or

Department of Neuropsychiatry, Oita University Faculty of Medicine, Yufu, Japan (J Akiyoshi MD); Department of Psychiatry, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan (N Horikawa MD); Department of Psychiatry, Osaka National Hospital, Osaka, Japan (H Hirotsune MD); Department of Psychiatry, Fukuoka University Faculty of Medicine, Fukuoka, Japan (N Eto MD); Department of Psychiatry, Fujita Health University School of Medicine, Toyoake, Japan (N Iwata MD); Department of Emergency Medicine, Tsukuba Medical Center Hospital, Tsukuba, Japan (M Kohno MD); Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan (M Mimura MD); and Department of Psychiatry, University of Tsukuba Graduate School of Comprehensive Human Sciences, Tsukuba, Japan (T Asada MD)

Correspondence to: Dr Chiaki Kawanishi, Health Management and Promotion Center, Yokohama City University Graduate School of Medicine, 22-2 Seto, Kanazawa-ku, Yokohama, Japan
chiaki.kawanishi@gmail.com

See Online for appendix

postcards, telephone calls, home visits, etc) to prevent repetition of suicide attempts.[7–17] However, no strong evidence has been produced for the effectiveness of this type of intervention.[18] In their systematic review,[19] O'Connor and colleagues showed that psychotherapy reduced suicide attempts in some high-risk adults in populations and settings relevant to primary care. In a randomised controlled trial,[12] cognitive therapy was effective at preventing suicide attempts in adults who had recently attempted suicide. However, the evidence overall is unclear, and the extent to which such findings are applicable to suicidal patients who are admitted to emergency departments is unknown.

Although most suicidal patients who are admitted to emergency departments are suffering from mental health problems, these patients often do not receive adequate mental health-care management in their communities after discharge.[20,21] In a randomised controlled trial, Morthorst and colleagues[22] examined the effects of assertive and intensive case management on repetition of suicide attempts, but the intervention did not lead to a significant reduction in this outcome; however, the study had a small sample size, patients were from a single centre, and individuals with psychosis were excluded from the study.

In this study, we aimed to investigate whether assertive and continuous case management could reduce the incidence of repetition of suicide attempts in adults with mental health problems who had attempted suicide, compared with enhanced usual care.

Methods

Study design and participants

ACTION-J was a multicentre, randomised controlled trial done at 17 Japanese hospitals (appendix) with both an emergency department and a psychiatric department. Potential study participants were adults (aged 20 years and older) who had attempted suicide and were admitted to the emergency department to receive critical care. To be eligible, patients had to have a primary diagnosis of an axis 1 psychiatric disorder, because the case management intervention was developed for patients with these disorders. Psychiatric diagnosis was obtained by structured interview with the Mini-International Neuropsychiatric Interview,[23] and defined as axis 1 in accordance with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR).[24] We excluded patients who had a primary diagnosis that did not meet the definition of a DSM-IV-TR axis 1 disorder.

Action in anticipation of death was confirmed at least twice in each patient by use of the Suicide Intent Scale.[25] Patients had to be able to understand the description of the study, provide informed consent, attend a face-to-face interview and a session for psychoeducation during their stay at the emergency department before enrolment in the study, and visit the participating hospital regularly to attend face-to-face interviews for assessments and case management after discharge from the emergency department.

The study protocol was approved by the Central Research Ethics Committee of the study sponsor (Japan Foundation for Neuroscience and Mental Health, Tokyo, Japan) and by the local ethics committees of all participating hospitals. All participants provided written informed consent.

Randomisation and masking

Participants were randomly assigned (1:1) by an internet-based system operated by a central, independent data centre to either the intervention group (assertive case management) or the control group (enhanced usual care). Assignment was by the minimisation method, with four factors: participating hospital, sex, age (younger than 40 years *vs* 40 years and older), and history of previous suicide attempts before the current episode. We regarded these as factors that could affect the study outcomes.

Outcome assessors were masked to group assignment, but patients and case managers who provided the interventions were not. The outcome assessors, who were trained for the assessments before the trial, collected the information about attempted suicide from participants or their family members by direct interview. The assessors did not know the participants' assigned groups, the status of implementation of the intervention, or information about events obtained by other on-site staff. An event review committee independently assessed all events related to the study outcomes.

Procedures

After patients were physically stabilised and alert consciousness was confirmed, potential study participants received thorough psychosocial assessment, including assessment of the social, psychological, and motivational factors specific to the self-harm event and an assessment of mental health, social risks, and needs, as recommended by UK national clinical practice guidelines.[26] Trained psychiatrists in the study group checked the patients against the inclusion and exclusion criteria, and provided a complete description of the study. Next, psychiatrists or other trained medical personnel from the study group gave the patients semi-structured psychoeducation, as suggested by WHO.[27] After the psychoeducation session, patients were provided with the complete study description again before being asked to provide informed consent. Assigned interventions were provided until the end of the follow-up period (ie, at least 18 months and up to 5 years).

Participants who were randomly assigned to the control group received enhanced usual care at the participating emergency departments.[28] In addition to the psychoeducation session in the emergency department before randomisation, these participants were given an information pamphlet listing available social resources (health care-based and local government services) every time they visited for periodic assessments (6 months and

18 months after randomisation, then annually until the end of the study).

Participants who were randomly assigned to the intervention group were offered assertive and continuous case management (panel 1), delivered by dedicated case managers who were trained experts in mental health (psychiatrists, nurses, social workers, or clinical psychologists). Encouragement to participate in psychiatric treatment was a core feature and appointments with psychiatrists and primary care physicians were organised. To facilitate the case management, the psychoeducation was also provided to participants' family members during the participants' initial stay in the hospital.

The case management was provided in accordance with a manual developed by the intervention programme committee of the study group. Briefly, the case managers periodically contacted participants assigned to the intervention group for 18 months after randomisation (at week 1 and at months 1, 2, 3, 6, 12, and 18) during their stay at the emergency department and after discharge. When applicable, the case managers contacted the participants every 6 months until the end of the trial (June 30, 2011). In principle, case management was accomplished through direct dialogue (face-to-face interviews by the case managers at the hospital), or by telephone conversation as the next best option. When case managers could not reach participants, they approached family members who had given their consent in advance to be contacted; the frequency with which this approach was used was not monitored. To maintain the quality of the standardised intervention, the intervention programme committee (which consisted of the case managers and a group of the study investigators) held case conference meetings every 2 months (fidelity scores were not calculated). The committee also visited the participating hospitals when necessary.

The protocol specified two interim analyses to assess the primary outcome, the first at roughly two-thirds into enrolment, and the second at the end of enrolment.[28] An independent data monitoring committee reviewed safety and efficacy issues from the interim analyses and from periodic monitoring reports

Panel 1: Features of the assertive case management intervention

- Periodic contact (either face-to-face or by telephone) with participants during their stay in the emergency department and after discharge
- Collection of information about each participant's treatment status and social problems that could disturb their treatment adherence
- Encouragement of participants to adhere to psychiatric treatment
- Coordination of appointments with psychiatrists and primary care physicians
- Encouragement of participants who discontinued psychiatric treatment to return to treatment
- Referrals to social services and private support organisations, and coordination for use of these resources to accommodate the individual needs of patients
- Provision of the psychoeducation content and information about social resources through a dedicated website

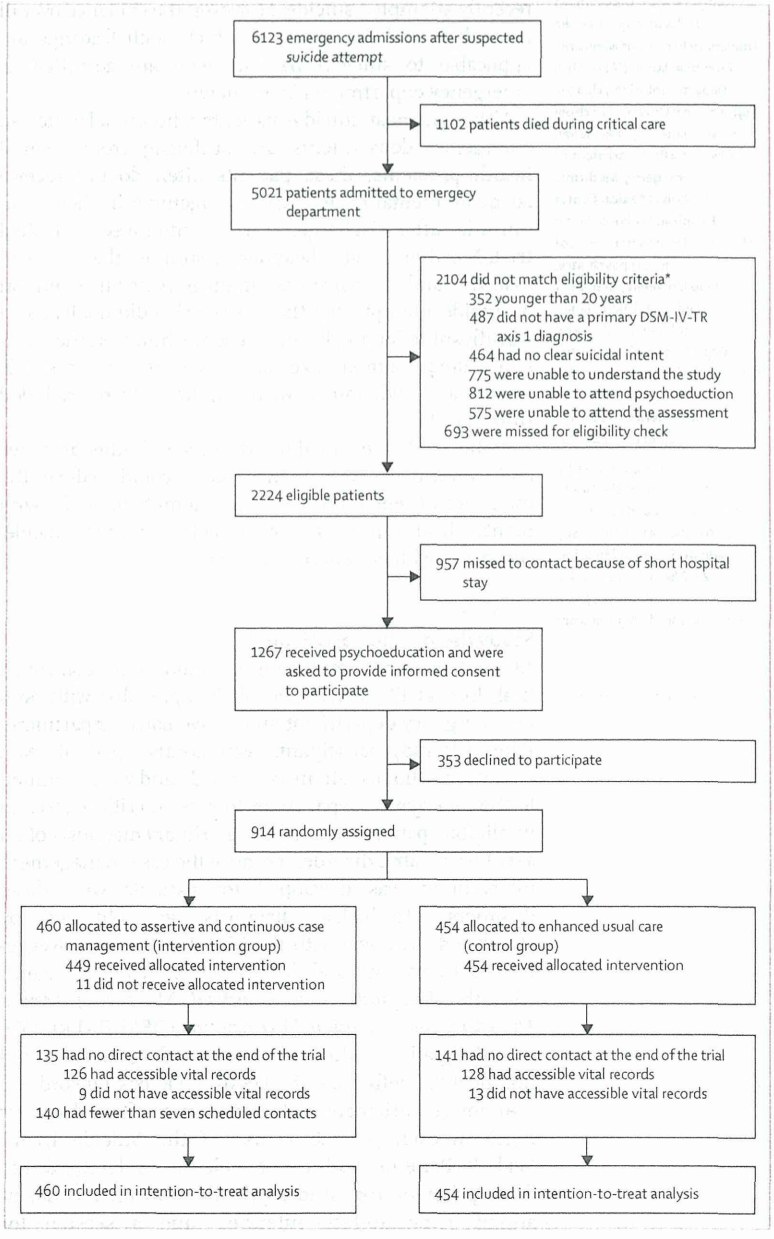

Figure 1: **Trial profile**
DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.[24] *Some participants were excluded for more than one reason.

	Assertive case management group (n=460)	Enhanced usual care group (n=454)
Women	263 (57%)	251 (55%)
Mean age (years)	42·9 (14·6)	41·7 (15·2)
Older than 65 years	42 (9%)	44 (10%)
Primary psychiatric diagnosis		
Substance-related disorder	19 (4%)	26 (6%)
Schizophrenia or other psychotic disorder	93 (20%)	86 (19%)
Mood disorder	215 (47%)	211 (46%)
Adjustment disorder	100 (22%)	91 (20%)
Other	33 (7%)	40 (9%)
Visited a psychiatrist within 1 month before the suicide attempt	260 (57%)*	257 (57%)
Visited a physician other than a psychiatrist within 1 month before the suicide attempt	151 (33%)†	135 (30%)
Education		
Less than high school	115 (25%)	108 (24%)
High school	229 (50%)	237 (52%)
Beyond high school	116 (25%)	109 (24%)
Employment status		
Employed	194 (42%)	206 (45%)
Unemployed	243 (53%)	220 (48%)
Retired	11 (2%)	16 (4%)
Student	11 (2%)	12 (3%)
Missing data	1 (<1%)	0
Marital status		
Married	180 (39%)	195 (43%)
Single	169 (37%)	183 (40%)
Divorced	94 (20%)	61 (13%)
Widowed	17 (4%)	15 (3%)
Lives with partner or family	113 (25%)	84 (19%)
Previous suicide attempts		
None	229 (50%)	235 (52%)
One or two times	131 (28%)	125 (28%)
Three or more times	100 (22%)	94 (21%)
Method of the present suicide attempt‡		
Drug overdose	326 (71%)	322 (71%)
Gas	31 (7%)	28 (6%)
Laceration	76 (17%)	71 (16%)
Jumping from a high place	10 (2%)	7 (2%)
Intentional traffic-related injury	55 (12%)	60 (13%)
Hanging	27 (6%)	26 (6%)
Other	21 (5%)	21 (5%)

Data are n (%) or mean (SD). *One individual with missing data excluded from percentage calculation. †Three individuals with missing data excluded from percentage calculation. ‡Totals are greater than 100% because some individuals used more than one method.

Table 1: **Baseline characteristics**

produced every 3 months throughout the study period (under masking).

Outcomes

The primary outcome measure was the incidence of first recurrent suicidal behaviour (attempted suicide or completed suicide). We also measured incidence of completed suicide and all-cause mortality as secondary outcomes to support the primary outcome measure. Because our data for the primary outcome presented time-dependent effects (the proportional hazard assumption did not hold), we also measured the cumulative incidence of the first episode of recurrent suicidal behaviour at 1, 3, 6, 12, and 18 months after randomisation as ad-hoc analyses. Information about participant deaths was obtained by the outcome assessors or from the Government death registry.

Other protocol-specified secondary outcomes were number and incidence of recurrent suicidal behaviours, including repeated suicidal attempts per person-year; number of self-harm behaviours; types and numbers of people or organisations to consult; other medical services (clinical visit or hospital admission); physical function; Beck Hopelessness Scale score;[29] and Health Survey for quality-of-life score (short form-36).[30] We plan to publish results for all these outcomes in a seperate report.

Statistical analysis

We estimated that the annual incidence of first recurrent suicidal behaviour would be 15% in the control group[28] and 10·5% in the intervention group. Based on these estimates, we calculated that the minimum number of participants needed per group to confirm the superiority of the assertive case management intervention (with an α of 0·05 and a statistical power of 90%) was 421. In anticipation of withdrawals and missing data, we aimed to recruit 910 participants to the study.

Analyses were done in accordance with the intention-to-treat principle. To check the assumption of proportional hazards for the primary outcome, we generated an overall cumulative incidence curve using the Kaplan-Meier method and log-plot. Because our data presented time-dependent effects (the proportional hazards assumption did not hold), the hazard ratio in the survival analysis was not appropriate as a measure of effects.[31] Therefore, we calculated risk ratios (RRs) with 95% CIs for cumulative incidence at five timepoints as ad-hoc analyses; for comparison with the results obtained from previous reports,[32] we selected months 1, 3, 6, 12, and 18 after randomisation. We set α at 0·008 for adjustment of multiplicity by the Bonferroni method.[31]

We did regression analyses for the calculated RRs.[33] We also made adjustments by using regression models with the randomisation factors: sex (male *vs* female), age (younger than 40 years *vs* 40 years and older), and history of previous suicide attempts before the current episode (yes *vs* no). In sensitivity analyses, we did multiple imputations for missing data (at the ad-hoc timepoints) and used regression models to adjust for the randomisation factors.[34]

We did prespecified subgroup analyses of the primary outcome (using the ad-hoc analyses for the five specified timepoints) by sex (male *vs* female), age (younger than 40 years *vs* 40 years and older), and history of previous suicide attempts before the current episode (yes *vs* no).

Because of the exploratory nature of the subgroup analyses, we did not make any adjustment for multiplicity. We also did a post-hoc regression analysis in each subgroup analysis to investigate the effect of the remaining randomisation factors (sex, age, and previous suicide attempts) on the primary outcome (by timepoints).

This study is registered at ClinicalTrials.gov (NCT00736918) and UMIN-CTR (C000000444).

Role of the funding source

Neither the funder nor the sponsor of the study had any role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Of 6123 emergency admissions after suspected suicide attempt at participating hospitals between July 1, 2006, to Dec 31, 2009, 914 participants were enrolled in the study, of which 460 were randomly assigned to the intervention group (assertive case management) and 545 to the control group (enhanced usual care; figure 1). Baseline characteristics were well balanced between the groups (table 1). As planned in the protocol, two interim analyses were done during the study period (October, 2007, and June, 2008). The results of these analyses were reviewed by the independent data monitoring committee, but conclusive findings were not obtained (data not shown) and the trial was continued until the end of the study period.

The assertive case management group had fairly good adherence to the intervention at the end of the trial (figure 1); 320 (70%) of 460 participants were contacted at least seven times by a case manager. 11 (1%) participants in the assertive case management group did not receive the intervention.

With respect to the primary outcome of incidence of first recurrent suicidal behaviour, there was no difference between the two groups at the end of the study; the survival curve for the assertive case management group was not significantly different from that for the control group (log-rank p=0·258, Wilcoxon p=0·103; figure 2). However, in the ad-hoc analyses at selected timepoints (done because the proportional hazards assumption was not met), the cumulative incidence of first recurrent suicidal behaviour was significantly lower in the intervention group than in the control group at 1, 3, and 6 months after randomisation, but not at 12 or 18 months (table 2).

With respect to the secondary outcomes assessed in support of the primary outcome, we did not identify any differences between the intervention and control groups for completed suicide (27 [6%] of 460 *vs* 30 [7%] of 454, log-rank p=0·660) or all-cause mortality (46 [10%] of 460 *vs* 42 [9%] of 454, log-rank p=0·698).

In the subgroup analyses, the intervention group had a significantly lower cumulative incidence of first recurrent suicidal behaviour in women (up to 18 months), and in participants younger than 40 years (up to 6 months), and those with a history of previous suicide attempts (up to 6 months). We noted no signficant effect of the intervention in the other subgroups, apart from participants with no history of previous suicide attempts at 6 months only (table 3).

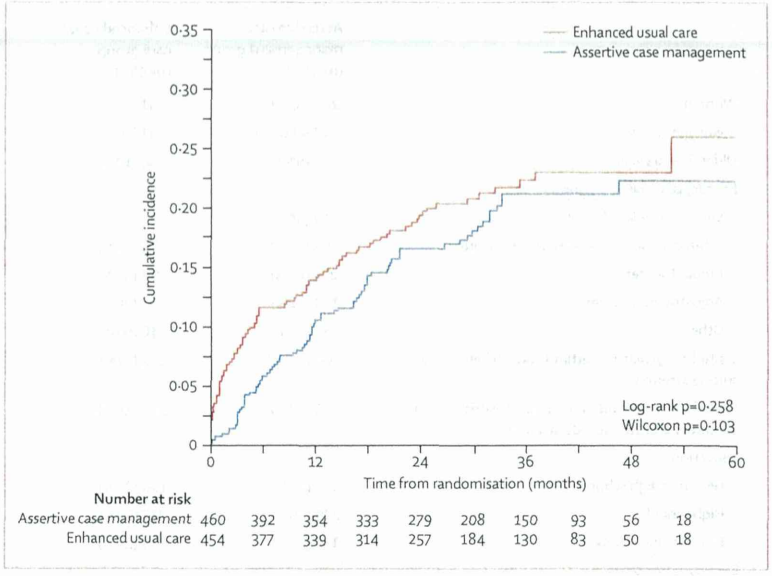

Figure 2: **Kaplan-Meier curve for incidence of first episode of recurrent suicidal behaviour (attempted suicide or completed suicide)**

In the sensitivity analysis for the primary analysis, which we did to investigate possible selection bias caused by missing data, we did not find any differences from the results obtained from the primary analysis when adjusted with randomisation factors (sex, age, and previous suicide attempts; table 2), nor from the results obtained from the subgroup analyses (table 3). The sensitivity analysis in the subgroup analysis, which we did to investigate possible selection bias caused by missing data, likewise showed no differences when adjusted for remaining randomisation factors (sex, age, and previous suicide attempts; table 3).

Discussion

Our results show that assertive and continuous case management based on psychiatric diagnoses, social risks, and needs of adults who had attempted suicide was not effective at reducing the risk of repetition of suicide attempt over the full study period (follow-up time from 18 months to 5 years dependent on time of entry to the study), but it did seem to be effective for up to 6 months in our ad-hoc analyses by time from randomisation (panel 2).

Our findings are partly consistent with the results of Morthorst and colleagues' randomised controlled trial in a single Danish hospital.[22] They implemented case management through assertive outreach with eight to 20 outreach consultations over 6 months by specialist nurses to

	1 month	3 months	6 months	12 months	18 months
Intervention vs control	3/444 (1%) vs 16/445 (4%)	7/430 (2%) vs 32/440 (7%)	25/417 (6%) vs 51/428 (12%)	43/397 (11%) vs 60/399 (15%)	55/380 (14%) vs 71/385 (18%)
Unadjusted risk ratio	0·19 (0·06–0·64)	0·22 (0·10–0·50)	0·50 (0·32–0·80)	0·72 (0·50–1·04)	0·79 (0·57–1·08)
Risk ratio (imputed)*	0·19 (0·05–0·63)	0·22 (0·10–0·48)	0·48 (0·31–0·77)	0·71 (0·49–1·02)	0·77 (0·55–1·06)
Risk ratio (adjusted)†	0·19 (0·05–0·60)	0·22 (0·10–0·49)	0·49 (0·31–0·77)	0·72 (0·50–1·04)	0·78 (0·57–1·07)
Risk ratio (imputed plus adjusted)‡	0·18 (0·05–0·60)	0·21 (0·09–0·47)	0·47 (0·30–0·75)	0·70 (0·48–1·00)	0·75 (0·54–1·03)

Data are number of events/population for the intervention (assertive case management) group or control (enhanced usual care) group, or risk ratio (95% CI). *Risk ratios with data imputed for individuals who missed the assessment. †Risk ratios adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode. ‡Risk ratios with data imputed for individuals who missed the assessment and adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode.

Table 2: **First recurrent suicidal behaviour (attempted suicide or completed suicide), by timepoint (ad-hoc analysis)**

improve adherence with after-treatment as an add-on to standard treatment. The intervention did not show a significant reduction of repetition of suicide attempt at 12 months (OR 0·69, 95%CI 0·34–1·43).

In our trial, adherence to the intervention was 70% (figure 1). After 6 months, the case management was provided every 6 months until the end of the follow-up period (ie, from 18 months to 5 years after randomisation), whereas before 6 months it was provided more often. The less frequent intervention after 6 months might have weakened the effectiveness of the intervention, although intervention might be effective only for a short period of time. Our results suggest that continuous case management needs to be taken over by community mental health caregivers within 6–12 months, dependent on the availability of medical and social resources in the community.

Because of the high adherence to our intervention programme and the fact that the trial design was embedded in real-world clinical settings, our study shows that the assertive case management intervention is feasible in clinical practice, with social workers or medical personnel playing the part of case managers. Our findings could also be relevant outside of Japan, in other countries with functioning emergency services and comprehensive mental health care services in place.

The subgroup analyses showed that greater effects were seen in women, participants younger than 40 years, and those with a history of previous suicide attempts. Patients attempting suicide constitute a heterogeneous group, differing in age, livelihood conditions, and risk factors. Further research is needed to examine why a greater effect was seen in these specific subgroups.

We noted no difference in the incidence of completed suicide between groups during the overall study period. In their randomised trial, Fleischmann and colleagues[15] reported significantly fewer deaths by suicide among people who had attempted suicide who were given brief intervention and contact than among those given treatment as usual at the 18-month follow-up. However, their trial was deliberately done in five low-resource countries with little infrastructure and scarce financial and human resources. They noted that treatment as usual for the participating sites in their study "would not cover routine or systematic psychiatric or psychological assessment or help", whereas in Japan psychiatric consultation was available at 76% of the registered tertiary emergency medical centres in 2012,[35] although only some of these centres provided routine psychiatric assessment.

Our study had some limitations. First, the enhancement of usual care might have affected the overall results of our study, since the control group received better care than is usual in clinical practice in Japan. We chose to use enhanced usual care as the comparison group for ethical reasons; however, this approach might have reduced the difference in the primary outcome between the assertive case management group and the control group.

Another limitation of our study is that it did not include suicidal patients younger than 20 years. These patients were excluded because individuals younger than 20 years are regarded as minors in Japan and informed consent has to be obtained from legal guardians. Additionally, we excluded suicidal patients without an axis 1 DSM-IV-TR disorder as their primary diagnosis because the intervention was designed specifically for patients with an axis 1 disorder.

Many individuals who had attempted suicide did not participate in the study because their physical conditions were too severe for them to understand the description of the study, and to attend the interview and session for psychoeducation. Additionally, we missed some people who had attempted suicide for eligibility review or contact for the informed consent because of their short hospital stay. Our results might have some selection bias; we could not collect data for people who did not participate in our study because of ethical restrictions. However, the characteristics of our study participants were similar to those described in a national registry study.[5]

Although the outcomes were systematically collected from participants and official records, our results might have some reporting bias. Additionally, we could not compare the self-reported outcome of suicidal behaviour by participants with register data for admissions to emergency wards for critical care or hospital contacts because it was impossible to track all register data or hospital contacts since the catchment areas of some emergency services in urban areas in Japan overlap, and

	1 month	3 months	6 months	12 months	18 months
Sex					
Men (n=400)					
Intervention vs control	2/190 (1%) vs 3/202 (1%)	4/184 (2%) vs 9/200 (5%)	10/178 (6%) vs 17/197 (9%)	18/172 (10%) vs 21/183 (11%)	24/168 (14%) vs 25/177 (14%)
Unadjusted risk ratio	0·69 (0·12–4·07)	0·48 (0·15–1·54)	0·65 (0·31–1·38)	0·91 (0·50–1·65)	1·01 (0·60–1·70)
Risk ratio (imputed)*	0·79 (0·13–4·66)	0·46 (0·14–1·46)	0·61 (0·29–1·29)	0·88 (0·48–1·61)	0·99 (0·59–1·67)
Risk ratio (adjusted)†	0·79 (0·13–4·66)	0·48 (0·15–1·52)	0·64 (0·30–1·36)	0·90 (0·50–1·62)	0·99 (0·60–1·66)
Risk ratio (imputed plus adjusted)‡	0·76 (0·13–4·48)	0·45 (0·14–1·44)	0·60 (0·28–1·27)	0·87 (0·48–1·57)	0·96 (0·57–1·62)
Women (n=514)					
Intervention vs control	1/254 (<1%) vs 13/243 (5%)	3/246 (1%) vs 23/240 (10%)	15/239 (6%) vs 34/231 (15)	25/225 (11%) vs 39/216 (18%))	31/212 (15%) vs 46/208 (22%)
Unadjusted risk ratio	0·07 (0·01–0·56)	0·13 (0·04–0·43)	0·43 (0·24–0·76)	0·62 (0·39–0·98)	0·66 (0·44–0·99)
Risk ratio (imputed)*	0·07 (0·01–0·56)	0·13 (0·04–0·41)	0·42 (0·24–0·75)	0·61 (0·38–0·98)	0·64 (0·42–0·98)
Risk ratio (adjusted)†	0·07 (0·01–0·54)	0·13 (0·04–0·41)	0·43 (0·24–0·76)	0·64 (0·40–1·00)	0·66 (0·44–0·99)
Risk ratio (imputed plus adjusted)‡	0·01 (0·04–0·55)	0·12 (0·04–0·40)	0·42 (0·24–0·74)	0·61 (0·38–0·96)	0·63 (0·42–0·95)
Age					
Younger than 40 years (n=453)					
Intervention vs control	0/216 vs 12/222 (5%)	3/210 (1%) vs 23/221 (10%)	14/204 (7%) vs 37/216 (17%)	27/193 (14%) vs 41/207 (20%)	32/186 (17%) vs 49/200 (25%)
Unadjusted risk ratio	..	0·14 (0·04–0·45)	0·40 (0·22–0·72)	0·71 (0·45–1·10)	0·70 (0·47–1·05)
Risk ratio (imputed)*	..	0·13 (0·04–0·43)	0·38 (0·21–0·69)	0·67 (0·43–1·05)	0·66 (0·44–0·99)
Risk ratio (adjusted)†	..	0·13 (0·04–0·43)	0·39 (0·22–0·69)	0·69 (0·44–1·07)	0·68 (0·46–1·01)
Risk ratio (imputed plus adjusted)‡	..	0·13 (0·04–0·42)	0·37 (0·21–0·67)	0·65 (0·41–1·01)	0·64 (0·43–0·96)
Older than 40 years (n=461)					
Intervention vs control	3/228 (1%) vs 4/223 (2%)	4/220 (2%) vs 9/219 (4%)	11/213 (5%) vs 14/212 (7%)	16/204 (8%) vs 19/192 (10%)	23/194 (12%) vs 22/185 (12%)
Unadjusted risk ratio	0·73 (0·17–3·24)	0·44 (0·14–1·41)	0·78 (0·36–1·68)	0·79 (0·42–1·50)	1·00 (0·58–1·73)
Risk ratio (imputed)*	0·72 (0·16–3·19)	0·43 (0·13–1·37)	0·76 (0·35–1·63)	0·81 (0·43–1·54)	1·01 (0·58–1·75)
Risk ratio (adjusted)†	0·81 (0·18–3·59)	0·45 (0·14–1·43)	0·80 (0·37–1·73)	0·81 (0·43–1·52)	0·99 (0·58–1·72)
Risk ratio (imputed plus adjusted)‡	0·78 (0·18–3·48)	0·43 (0·13–1·38)	0·77 (0·36–1·67)	0·82 (0·43–1·54)	1·00 (0·57–1·74)
Previous suicide attempt					
None (n=464)					
Intervention vs control	1/223 (<1%) vs 3/234 (1%)	3/216 (1%) vs 10/230 (4%)	7/207 (3%) vs 19/220 (9%)	14/202 (7%) vs 21/204 (10%)	17/192 (9%) vs 24/198 (12%)
Unadjusted risk ratio	0·35 (0·04–3·34)	0·32 (0·09–1·15)	0·39 (0·17–0·91)	0·67 (0·35–1·29)	0·73 (0·41–1·32)
Risk ratio (imputed)*	0·34 (0·04–3·27)	0·31 (0·09–1·10)	0·38 (0·16–0·88)	0·68 (0·36–1·31)	0·73 (0·40–1·32)
Risk ratio (adjusted)†	0·36 (0·04–3·40)	0·33 (0·09–1·18)	0·41 (0·18–0·95)	0·70 (0·37–1·34)	0·75 (0·42–1·34)
Risk ratio (imputed plus adjusted)‡	0·35 (0·04–3·32)	0·32 (0·09–1·13)	0·39 (0·17–0·91)	0·70 (0·37–1·34)	0·73 (0·41–1·33)
One or more (n=450)					
Intervention vs control	2/221 (1%) vs 13/211 (6%)	4/214 (2%) vs 22/210 (10%)	18/210 (9%) vs 32/208 (15%)	29/195 (15%) vs 39/195 (20%)	38/188 (20%) vs 47/187 (25%)
Unadjusted risk ratio	0·15 (0·03–0·64)	0·18 (0·06–0·51)	0·56 (0·32–0·96)	0·74 (0·48–1·15)	0·80 (0·55–1·17)
Risk ratio (imputed)*	0·15 (0·03–0·64)	0·17 (0·06–0·49)	0·53 (0·31–0·92)	0·71 (0·45–1·10)	0·77 (0·52–1·12)
Risk ratio (adjusted)†	0·14 (0·03–0·61)	0·17 (0·06–0·49)	0·53 (0·31–0·91)	0·73 (0·57–1·12)	0·78 (0·54–1·14)
Risk ratio (imputed plus adjusted)‡	0·14 (0·03–0·62)	0·17 (0·06–0·48)	0·51 (0·30–0·88)	0·69 (0·44–1·06)	0·74 (0·51–1·09)

Data are number of events/population for the intervention (assertive case management) group or control (enhanced usual care) group, or risk ratio (95% CI). *Risk ratios with data imputed for individuals who missed the assessment. †Risk ratios adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode. ‡Risk ratios with data imputed for individuals who missed the assessment and adjusted by use of regression models for the randomisation factors of sex, age, and history of previous suicide attempts before the current episode.

Table 3: **First recurrent suicidal behaviour (attempted suicide or completed suicide), by subgroup (ad-hoc analysis by timepoint)**

Panel 2: Research in context

Systematic review

We searched PubMed for articles published from Jan 1, 1949, to Feb 28, 2014, using the search terms "suicid*" OR "self-harm" OR "self-injury" AND "random*" OR "interventions". We identified 12 relevant systematic reviews of randomised trials; the most recent systematic review was by O'Connor and colleagues,[19] which showed that psychotherapy reduced suicide attempts in some high-risk adults in populations and settings relevant to primary care. In a recent randomised trial, Morthorst and colleagues[22] examined the effects of assertive and intensive case management on repetition of suicide attempt, but the intervention did not lead to a significant reduction in repetition of suicide attempt.

Interpretation

In our large, multicentre, randomised controlled trial assertive case management was feasible in real-world clinical settings for suicidal patients with psychiatric disorders admitted to the emergency department. Although it was not effective at reducing the incidence of repetition of suicide attempts in the long term, the results of our ad-hoc analyses suggested that it was effective for up to 6 months. Our results also suggest potentially heterogeneous effects of assertive case management; the intervention seemed to be more effective in women, participants younger than 40 years, and those with a history of previous suicide attempts.

some participants might have moved out of the catchment areas. Finally, although outcome data were collected by trained assessors, possible variability of the assessments might have introduced bias into the results.

Contributors

YHir, CK, TA, NI, and NY conceived and designed the study. YHir was the principal investigator. YHir, CK, KO, YO, KI, AS, HM, YHit, AIwak, TK, JA, NH, HH, NE, NI, MK, AIwan, MM, and TA enrolled patients. YHir, CK, KO, YK, YO, KI, AS, HM, YHit, AIwak, TK, JA, NH, HH, NE, NI, MK, AIwan, MM, and TA managed the study at the participating sites. NI and NY analysed the data. CK wrote the first draft of the report. YHir, TA, KO, YK, YO, KI, AS, HM, YHit, AIwak, TK, JA, NH, HH, NE, NI, MK, AIwan, MM, and TA contributed to the writing of the report.

Declaration of interests

We declare no competing interests.

Acknowledgments

This study was funded by the Ministry of Health, Labour, and Welfare of Japan. We thank the participating hospitals for their cooperation. We thank Mitsuhiko Yamada and Masatoshi Inagaki from the National Center of Neurology and Psychiatry (Tokyo, Japan) for their helpful assistance. We also thank Navneet Kapur from the University of Manchester (Manchester, UK) for providing comments on the report. Finally, we express our deepest sorrow for the loss of Toshiharu Fujita, who greatly contributed to the design of this trial.

References

1 Isometsä ET, Lönnqvist JK. Suicide attempts preceding completed suicide. *Br J Psychiatry* 1998; **173:** 531–35.
2 Da Cruz D, Pearson A, Saini P, et al. Emergency department contact prior to suicide in mental health patients. *Emerg Med J* 2011; **28:** 467–71.
3 Nordentoft M, Mortensen PB, Pedersen CB. Absolute risk of suicide after first hospital contact in mental disorder. *Arch Gen Psychiatry* 2011; **68:** 1058–64.
4 Hawton K, Bergen H, Casy D, et al. Self-harm in England: a tale of three cities. *Soc Psychiatry Psychiatr Epidemiol* 2007 **42:** 513–21.
5 Ting SA, Sullivan AF, Boudreaux ED, Miller I, Camargo CA Jr. Trends in US emergency department visits for attempted suicide and self-inflicted injury, 1993–2008. *Gen Hosp Psychiatry* 2012; **24:** 557–65.
6 D'Onofrio G, Jauch E, Jagoda A, et al. NIH roundtable on opportunities to advance research on neurologic and psychiatric emergencies. *Ann Emerg Med* 2010; **56:** 551–64.
7 Gibbons JS, Butler J, Urwin P, Gibbons JL. Evaluation of a social work service for self-poisoning patients. *Br J Psychiatry* 1978; **133:** 111–18.
8 Allard R, Marshall M, Plante MC. Intensive follow-up does not decrease the risk of repeat suicide attempts. *Suicide Life Threat Behav* 1992; **22:** 303–14.
9 van Heeringen C, Jannes S, Buylaert W, Henderick H, De Bacquer D, van Remoortel J. The management of non-compliance with referral to out-patient after-care among attempted suicide patients: a controlled intervention study. *Psychol Med* 1995; **25:** 963–70.
10 van der Sande R, van Rooijen L, Buskens E, et al. Intensive in-patient and community intervention versus routine care after attempted suicide. A randomised controlled intervention study. *Br J Psychiatry* 1997; **171:** 35–41.
11 Cedereke M, Monti K, Öjehagen A. Telephone contact with patients in the year after a suicide attempt: does it affect treatment attendance and outcome? A randomised controlled study. *Eur Psychiatry* 2002; **17:** 82–91.
12 Brown GK, Have TT, Henriques GR, Xie SX, Hollander JE, Beck AT. Cognitive therapy for the prevention of suicide attempts. *JAMA* 2005; **294:** 563–70.
13 Vaiva G, Vaiva G, Ducrocq F, et al. Effect of telephone contact on further suicide attempts in patients discharged from an emergency department: randomised controlled study. *BMJ* 2006; **332:** 1241–45.
14 Carter GL, Clover K, Whyte IM, Dawson AH, D'Este C. Postcards from the EDge: 24-month outcomes of a randomised controlled trial for hospital-treated self-poisoning. *Br J Psychiatry* 2007; **191:** 548–53.
15 Fleischmann A, Bertolote JM, Wasserman D, et al. Effectiveness of brief intervention and contact for suicide attempters: a randomized controlled trial in five countries. *Bull World Health Organ* 2008; **86:** 703–09.
16 Beautrais AL, Gibb SJ, Faulkner A, Fergusson DM, Mulder RT. Postcard intervention for repeat self-harm: randomised controlled trial. *Br J Psychiatry* 2010; **197:** 55–60.
17 Hassanian-Moghaddam H, Sarjami S, Kolahi A, Carter GL. Postcards in Persia: randomised controlled trial to reduce suicidal behaviours 12 months after hospital-treated self-poisoning. *Br J Psychiatry* 2011; **198:** 309–16.
18 Kapur N, Cooper J, Bennewith O, Gunnel D, Hawton K. Postcards, green cards and telephone calls: therapeutic contact with individuals following self-harm. *Br J Psychiatry* 2010; **197:** 5–7.
19 O'Connor EA, Gaynes BN, Burda BU, Soh C, Whitlock EP. Screening for and treatment of suicide risk relevant to primary care: a systematic review for the US Preventive Service Task Force. *Ann Intern Med* 2013; **158:** 741–54.
20 Gairin I, House A, Owens D. Attendance at the accident and emergency department in the year before suicide: retrospective study. *Br J Psychiatry* 2003; **183:** 28–33.
21 Olfson M, Marcus SC, Bridge JA. Emergency treatment of deliberate self-harm. *Arch Gen Psychiatry* 2012; **69:** 80–88.
22 Morthorst B, Krogh J, Erlangsen A, Alberdi F, Nordentoft M. Effect of assertive outreach after suicide attempt in the AID (assertive intervention for deliberate self harm) trial: randomised controlled trial. *BMJ* 2013; **345:** e4972.
23 Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuro-mental Interview (MINI): the development and validation of a structured diagnostic mental interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998; **59:** 22–33.
24 American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth edition, text revision. Washington, DC: American Psychiatric Association, 2000.
25 Beck A, Schuyler D, Herman, J. Development of suicidal intent scales. In: Beck A, Resnik H, Lettieri DJ, eds. The prediction of suicide. Bowie: Charles Press, 1975: 45–56.

26 National Collaborating Centre for Mental Health. Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care. In: National Clinical Practice Guideline Number 16. Leicester and London: British Psychological Society and Royal College of Psychiatrists, 2004.

27 WHO. Multisite intervention study on suicidal behaviours SUPRE-MISS: protocol of SUPREMISS. Geneva: World Health Organization, 2002.

28 Hirayasu Y, Kawanishi C, Yonemoto N, et al. A randomized controlled multicenter trial of post-suicide attempt case management for the prevention of further attempts in Japan (ACTION-J). *BMC Public Health* 2009; **9**: 364.

29 Beck AT, Brown G, Berchick RJ, Stewart BL, Steer RA. Relationship between hopelessness and ultimate suicide: a replication with psychiatric outpatients. *Am J Psychiatry* 1990; **147**: 190–95.

30 Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol* 1998; **51**: 913–23.

31 Chow S-C, Liu J-P. Design and analysis of clinical trials: concept and methodologies, 2nd edn. Hoboken: Wiley, 2004.

32 Hawton K, Townsend E, Arensman E, et al. Psychosocial versus pharmacological treatments for deliberate self harm. *Cochrane Database Syst Rev* 2000; **2**: CD001764.

33 McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol* 2003; **157**: 940–43.

34 Carpenter J, Kenward M. Multiple imputation and its application. Hoboken: Wiley, 2013.

35 Ministry of Health, Labour, and Welfare of Japan. Survey of tertiary emergency medical centers in Japan (in Japanese). http://www.mhlw.go.jp/stf/shingi/2r985200000335ux-att/2r9852000003361c.pdf (accessed July 1, 2014).

Journal of Affective Disorders 175 (2015) 66–78

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Special review article

Interventions to prevent repeat suicidal behavior in patients admitted to an emergency department for a suicide attempt: A meta-analysis

Masatoshi Inagaki [a,*], Yoshitaka Kawashima [b], Chiaki Kawanishi [c], Naohiro Yonemoto [b], Tatsuya Sugimoto [d], Taku Furuno [e], Katsumi Ikeshita [f], Nobuaki Eto [g], Hirokazu Tachikawa [h], Yohko Shiraishi [i], Mitsuhiko Yamada [b]

[a] Department of Neuropsychiatry, Okayama University Hospital, Japan
[b] Department of Neuropsychopharmacology, National Institute of Mental Health, National Center of Neurology and Psychiatry, Japan
[c] Health Management and Promotion Center, Yokohama City University Graduate School of Medicine, Japan
[d] Department of Psychiatry, Tokyo Metropolitan Matsuzawa Hospital, Japan
[e] Department of Psychiatry, National Hospital Organization Yokohama Medical Center, Japan
[f] Department of Psychiatry, Psychiatric Institute, Nara Medical University, Japan
[g] Department of Psychiatry, Faculty of Medicine Fukuoka University, Japan
[h] Department of Psychiatry, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Japan
[i] Department of Psychiatry, Yokohama City University School of Medicine, Japan

ARTICLE INFO

Article history:
Received 4 August 2014
Received in revised form
12 December 2014
Accepted 19 December 2014
Available online 30 December 2014

Keywords:
Suicide
Self-harm
Emergency department
Meta-analysis
Systematic review

ABSTRACT

Background: A huge number of patients with self-harm and suicide attempt visit emergency departments (EDs). We systematically reviewed studies and examined the effect of interventions to prevent repeat suicidal behavior in patients admitted to EDs for a suicidal attempt.
Method: We searched the databases of MEDLINE, PsychoINFO, CINAHL, and EMBASE through August 2013. Eligible studies were randomized controlled trials assessing the effects on repeat suicidal behavior of interventions initiated in suicidal patients admitted to EDs. Interventions in each trial were classified into groups by consensus. Meta-analyses were performed to determine pooled relative risks (RRs) and 95% confidence intervals (CIs) of repetition of suicide attempt for interventions in each group.
Results: Out of 5390 retrieved articles, 24 trials were included and classified into four groups (11 trials in the Active contact and follow-up, nine in the Psychotherapy, one in the Pharmacotherapy, and three in the Miscellaneous). Active contact and follow-up type interventions were effective in preventing a repeat suicide within 12 months (n=5319; pooled RR=0.83; 95% CI: 0.71 to 0.97). However, the effect at 24 months was not confirmed (n=925; pooled RR=0.98; 95% CI: 0.76–1.22). The effects of the other interventions on preventing a repetition of suicidal behavior remain unclear.
Limitation: Caution is needed regarding the heterogeneity of the effects.
Conclusion: Interventions of active contact and follow-up are recommended to reduce the risk of a repeat suicide attempt at 12 months in patients admitted to EDs with a suicide attempt. However, the long-term effect was not confirmed.

Contents

* Correspondence to: Department of Neuropsychiatry, Okayama University Hospital, 2-5-1, Shikata-cho, Kita-ku, Okayama, 700-8558, Japan Tel.: +81 86 235 7242; fax: +81 86 235 7246.
E-mail address: masatoshiinagaki@okayama-u.ac.jp (M. Inagaki).

http://dx.doi.org/10.1016/j.jad.2014.12.048
0165-0327/