

Effectiveness of a Multimodal Community Intervention Program to Prevent Suicide and Suicide Attempts: A Quasi-Experimental Study

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Abstract

Background: Multilevel and multimodal interventions have been suggested for suicide prevention. However, few studies have reported the outcomes of such interventions for suicidal behaviours.

Methods: We examined the effectiveness of a community-based multimodal intervention for suicide prevention in rural areas with high suicide rates, compared with a parallel prevention-as-usual control group, covering a total of 631,133 persons. The effectiveness was also examined in highly populated areas near metropolitan cities (1,319,972 persons). The intervention started in July 2006, and continued for 3.5 years. The primary outcome was the incidence of composite outcome, consisting of completed suicides and suicide attempts requiring admission to an emergency ward for critical care. We compared the rate ratios (RRs) of the outcomes adjusted by sex, age group, region, period and interaction terms. Analyses were performed on an intention-to-treat basis and stratified by sex and age groups.

Findings: In the rural areas, the overall median adherence of the intervention was significantly higher. The RR of the composite outcome in the intervention group decreased 7% compared with that of the control group. Subgroup analyses demonstrated heterogeneous effects among subpopulations: the RR of the composite outcome in the intervention group was significantly lower in males (RR = 0.77, 95% CI 0.59–0.998, p = 0.0485) and the RR of suicide attempts was significantly lower in males (RR = 0.39, 95% CI 0.22–0.68, p = 0.001) and the elderly (RR = 0.35, 95% CI 0.17–0.71, p = 0.004). The intervention had no effect on the RR of the composite outcome in the highly populated areas.

Interpretation: Our findings suggest that this community-based multimodal intervention for suicide prevention could be implemented in rural areas, but not in highly populated areas. The effectiveness of the intervention was shown for males and for the elderly in rural areas.

Trial Registration: ClinicalTrials.gov NCT00737165 UMIN Clinical Trials Registry UMIN000000460

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Introduction

Suicide is a devastating event for individuals, families, and communities. The World Health Organization estimates that nearly 1,000,000 people worldwide die from suicide every year. [1] Several reviews have indicated that multilevel and multimodal interventions would be the strategy of choice for suicide prevention in the community. [2–4] A synergistic effect between interventions would be theoretically possible. [4] However, the low rate of suicide in the general population has made it difficult for trials to detect differences between groups with statistical power. Indeed, there are few studies that have reported the effect of interventions on suicide rates. [2–4].

We examined the effectiveness of a community-based multimodal intervention for suicide prevention in rural areas where the suicide rate was high, with a non-randomised comparative intervention trial using parallel prevention-as-usual control. The effectiveness was also examined in highly populated areas near metropolitan cities. In the study, a large population size and an appropriate observational period to observe enough suicidal behaviour, and thus to obtain enough statistical power, were used. In addition, preplanned subgroup analyses were performed to detect effects of the intervention in specific subpopulations.

Methods

Study Designs

We set two areas, rural areas and highly populated areas, as the study targets (Figure 1). Rural areas with a high suicide rate were the primary targets, because these were the areas of focus in the previous community interventions in Japan, which are the basis of

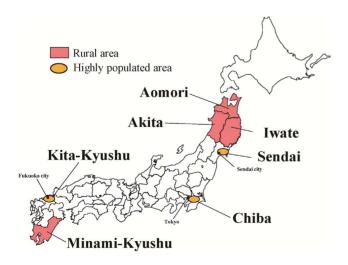


Figure 1. Location map of the study areas. Pink-coloured areas indicate rural study areas. Orange-coloured areas indicate highly populated study areas. doi:10.1371/journal.pone.0074902.g001

the interventions in the present study. [5–7] The entire population was the target of the intervention. The study matched pairs of intervention groups and control groups with past suicide rates and population size. The participants in the rural areas were the inhabitants living in four matched pairs of intervention groups and control groups (consisting of 17 communities, Figure 2). Highly populated areas near metropolitan cities were another target in this study because the suicide rate in these areas had increased prior to the present study. [8] In highly populated areas, two neighbouring communities were designated as the intervention and control groups, respectively. The participants in the highly populated areas were the inhabitants living in three matched pairs of intervention group and control group (consisting of six communities, Figure 2).

A community-based multimodal intervention for suicide prevention was developed [9] by extending the findings from previous studies focused on depressive elderly living in rural areas of Japan. [5–7] The intervention intended to reinforce human relationships and connectedness in the community by focusing on building social support networks within the general public and the healthrelated resources. The essential components are listed in Table 1. As shown here, the intervention was multilevel and multimodal, targeting the entire population in the participating communities. Leadership involvement was an important factor for the effective implementation of long-term programs by creating society commitment at multiple levels and establishing community support networks. Education and awareness programs aimed to reduce the stigmatisation of mental illness and suicide. The programs also aimed at improving the recognition of suicide risk and facilitating help-seeking and access to mental health services through improved understanding of the causes and risk factors for suicidal behaviour. Training programs targeting gatekeepers and care providers aimed to facilitate their roles in early detection within potentially vulnerable populations and to increase preventive functions. The screening programs aimed to identify at-risk individuals in the community and direct them to treatment. In addition, the program recommended that the local health authorities provide appropriate care for suicide survivors to support their grief work, if necessary.

Local governments and the local health authorities collaborated and implemented the intervention programs in accordance with the manual (in Japanese; www.mhlw.go.jp/seisakunitsuite/bunya/ hukushi_kaigo/shougaishahukushi/jisatsu/index.html,) developed by the program committee of the NOCOMIT-J group. They implemented the intervention with their own budgets. The participants were not blind to the intervention, which started in July 2006. As short duration interventions did not seem to have any detectable effect [2], the intervention continued for 3.5 years. The intervention in the control group was suicide prevention activities as usual. The list of the programs was opened to the control group when the heads of the local governments agreed to participate in this trial. However, we did not show them the detailed intervention manual. The study monitoring and the data collection were conducted in both the intervention group and control group.

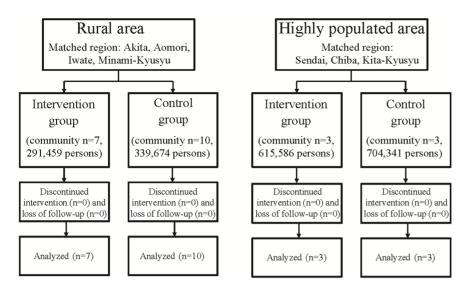


Figure 2. Flow chart of the study. doi:10.1371/journal.pone.0074902.g002

The primary outcome was the incidence of composite outcome, consisting of completed suicides and suicide attempts that required admission to an emergency ward for critical care. Secondary outcomes were as follows: 1) incidence of completed suicides, 2) incidence of suicide attempts that required admission to an emergency ward for critical care, and 3) proportion of adherence with the required components of the intervention described in the manual. For the adherence assessments, information regarding the implementation of the programs described in the manual was collected every 6 months from the month when the study started in all participating regions. The binary questions for the adherence items were prepared based on the essential components listed in Table 1 and were collected from the local health authorities. The reporters of events were not blind to the intervention. Death certificates from the Vital Statistics Records (Ministry of Health, Labour, and Welfare, Japan) for the participating regions from 2003 to 2009 were used every year to collect the following data items: International Classification of Diseases 10th Revision code for intentional selfharm (ICD-10 codes X60-X84), sex, age, and region code. In this study, a suicide attempt patient was defined as a self-harmed individual transported by regional ambulance service and admitted to an emergency ward for critical care. In Japan, fees for ambulance services are covered by the National Health Insurance System, which allows virtually all suicide attempters access to emergency medicine when requested. The following information was collected from the Regional Ambulance Services every 6 months from 2003 to 2009: type of transportation, date of notification, region code, severity, sex and age. Therefore, the data on suicide attempts systematically collected in this study were reliable. The total population numbers by the community, sex and age groups were collected every year from the National Basic Resident Registration System.

Statistical Analysis

In the primary analysis, we compared the rate ratios (RRs) of incidence of the composite outcome as adjusted by covariates for the effect of the intervention. Marginal models (link function; log, distribution; Poisson) with generalised estimating equations [10] were used to examine the effect of the intervention adjusted by sex,

age group (under 25, 25–65, over 65 years), region, period (6-month) and interaction terms (interventions × periods). These variables are well known risk factors from past epidemiological studies and they serve as effect modifications in interventional studies. [11] On the other hand, it takes some time to set up and implement the intervention programs in the community. Therefore, the effects of the intervention would be time-dependent. The 6-month periods were chosen to minimise varying populations. The analysis calculated RRs and their 95% confidence intervals (CI). We conducted an interim analysis 2 years after starting to evaluate the achievement of the primary objective. Therefore, the significance level in the final analysis was set at 0.0492 for the two-sided test based on the method of O'Brien and Fleming. [12].

Sample sizes to be used in the study were calculated based on the assumptions of the suicide rates from 2002 to 2004 in the participating regions. Although the estimated sample sizes were not adjusted for sex, age groups and regions, if all assumptions were met, the statistical power would be over 80%. [9].

Secondary outcomes were analysed to examine whether the rates of completed suicides and suicide attempts were significantly reduced in the intervention group when compared with those of the control group, respectively. Adherence to the interventions was also examined.

Preplanned subgroup analyses of the primary and secondary outcomes by sex and age groups (under 25, 25–65, over 65) were performed. Because these variables were the known risk factors and effect modifications, we also used them for the modelling in the primary analysis. No multiplicity adjustments were made, given the exploratory nature of the analyses.

All analyses were done on an intention-to-treat basis. Statistical analyses were performed using SAS version 9.2 software (SAS Institute Inc., Cary, North Carolina).

The study protocol was approved by the Central Research Ethics Committee of Japan Foundation for Neuroscience and Mental Health. The protocol was also approved by the local Ethics Committees of affiliated universities or institutes in the participating regions. (Aomori region: Kuroishi General Hospital Ethics Committee (http://hospital-kuroishi.jp/) and Hirosaki University Ethics Committee (http://www.hirosaki-u.ac.jp/), Akita region: Akita University Ethics Committee (http://www.akita-u.ac.jp/)

Table 1.

	Intervention Level	Target	Objectives and Actions
1	Leadership involvement	Local government	Leadership involvement is a key to effectively implementing long-term programs that utilize a commitment of society at multiple levels and succeed in establishing community support networks. Messages from the mayor have a strong impact on the efficiency of community development and community networking.
			a) Publicizing messages from the mayor to all officials and citizens reminding them of the importance o suicide prevention.
			b) Establishing a regional committee dedicated to suicide prevention chaired by the mayor to promote organization-wide awareness of mental health and suicide prevention and facilitate the collaboration of different sections of the local government.
			c) Formalizing the roles of each service section and promoting pathways to build social support networks within the public and health-related resources, intending to reinforce human relationships and connectedness in the community.
2	Education and awareness programs	Public	The education and awareness programs aim to reduce stigmatization of mental illness and suicide and to improve recognition of suicide risk and facilitation of help seeking.
			 a) Waging a campaign for general public education (public events, posters, websites, placards, leaflets and brochures with information about help available locally, self-tests, warning signals and treatment options and announcements of regional educational activities like lectures and seminars).
			b) Providing regional educational opportunities like lectures and seminars to improve understanding o the causes and risk factors for suicidal behavior, particularly mental illness. The programs also cover awareness of availability of social resources and referral procedures for people potentially at risk.
3	Gatekeeper training	Community or organizational gatekeepers	Training programs targeting gatekeepers (community leaders, priests, telephone hotlines, social services, youth workers, geriatric care providers, police, physicians, nurses, pharmacists, mental health providers, and those employed in institutional settings, such as schools) aimed to facilitate their playing important roles in early detection within potentially vulnerable populations and increasing preventive functions. These programs also promote organization-wide awareness of mental health and suicide and facilitate access to mental health services.
			 a) Training community or organizational gatekeepers to provide them with an opportunity to identify at-risk individuals within different target populations and direct them to appropriate social and/or mental health services.
4	Supporting individuals at high risk	Individuals at high risk	Home visiting and regional social gatherings aim to reinforce human relationships and connectedness in the community. Screening aims to identify at-risk individuals and direct them to treatment.
			a) Home visiting by regional public health nurses and psychiatrists.
			b) Setting up regional social gatherings.
			c) Screening to identify at-risk individuals and direct them to treatment or follow-up care providers. The focus may be on suicidal behavior directly or on risk factors, such as depression or substance abuse.
			d) Support for self-help activities for high-risk groups, i.e., suicide attempters, to facilitate access to professional help.

*The intervention programs focused on building social support networks within the general public and in health-related resources, intending to reinforce human relationships and connectedness in the community.

honbu/), Iwate region: Iwate University Ethics Committee (http://www.iwate-med.ac.jp/), Minami-Kyusyu region: Keio University Ethics Committee (http://www.med.keio.ac.jp/), Sendai region: Tohoku Bunka Gakuen University Ethics Committee (http://www.tbgu.jp/univ/) and Sendai City Hospital Ethics Committee (http://hospital.city.sendai.jp/), Chiba region: National Center Of Neurology And Psychiatry Ethics Committee (http://www.ncnp.go.jp/), Kita-Kyusyu region: University of Occupational And Environmental Health Ethics Committee (http://www.uoeh-u.ac.jp/JP/index.html). We did not directly contact all participants and collect data from all individuals (all data were anonymous) in this study. Therefore, we did not obtain written informed consent from individuals living in the participating regions. Instead, the regional investigators obtained the written authorisation to conduct the study from the head of the local governments on behalf of all inhabitants and announced it as verbal consent in all by public publications in the participated

regions. The processes approved the Central Research Ethics Committee and the local Ethics Committees and complied with the Ethical Guidelines for Epidemiology Research (published by the Ministry of Health, Labour, and Welfare, Japan, http://www.niph.go.jp/wadai/ekigakurinri/guidelines.pdf).

The present study is in accordance with the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) statement [13,14] and the trial protocol was registered at ClinicalTrials.gov (NCT00737165) and UMIN-CTR (UMIN000000460).

Role of the Funding Source

The study was conceived and developed by the NOCOMIT-J group, and was funded by the Ministry of Health, Labour, and Welfare of Japan. The Japan Foundation for Neuroscience and Mental Health was the sponsor. Neither the funder nor the sponsor had any role in study design, data collection, data analysis,

^{**}A suicide leaves behind more victims than just the individual, as family, friends, co-workers, and the community can be impacted in many different and unique ways following a suicide. In this study, the program recommended that the local government provide appropriate care for suicide survivors (a person who survives a suicide completer; a suicide griever) to support their grief work, if necessary. Support the activities of self-help groups for suicide survivors and other related organizations. doi:10.1371/journal.pone.0074902.t001

data interpretation, or writing of the report. YO made the final decision to submit for publication.

Results

Demographic Information of the Participating Regions

The trial flow chart is shown in Figure 2. Population characteristics of the participating areas at baseline are shown in Table 2. In the rural study areas, the total population was 631,133 in 2006. In the highly populated study areas, the total population was 1,319,972 in 2006. Numbers of completed suicides, suicide attempts requiring admission to an emergency ward for critical care, and populations from 2003 to 2009 in the rural areas and the highly populated areas are listed in Table 3 and Table 4, respectively.

The adherence to the suicide prevention programs implemented in the participating areas is shown in Figure 3 and 4. In rural areas, the overall median adherence of the intervention group was 0.65 and significantly higher than that obtained from the control group (beta = 0.42, 95% CI 0.12–0.72, p = 0.0056). On the other hand, in highly populated areas, the overall median adherence of the intervention group was 0.55, not different from that of the control group (beta = 0.35, 95% CI -0.01-0.71, p = 0.0552).

The interim analysis conducted 2 years after the start of the intervention demonstrated that the incidence rates of the composite outcome were similar between the intervention group and control group in the rural areas (RR = 0.99, 95% CI 0.79-1.06, p = 0.257). As the result, the study was continued until the end of the planned period.

As shown in Figure 5, in the rural areas the incidence rates of the composite outcome in the intervention group were slightly lower than those obtained from the control group $(RR=0.93,\ 95\%\ CI\ 0.71-1.22,\ p=0.598)$. A subgroup analysis

demonstrated that the incidence rates in the intervention group were significantly lower in males (RR = 0.77, 95% CI 0.59–0.998, p=0.0485). Also, the analysis demonstrated that the incidence rates in the intervention group were lower in the elderly over 65 years old (RR = 0.76, 95% CI 0.57–1.01, p=0.062), while the incidence rates were higher in females (RR = 1.34, 95% CI 0.87–2.15, p=0.174) and in participants younger than 25 years old (RR = 1.44, 95% CI 0.63–3.31, p=0.386).

In the highly populated areas, the incidence rates of the composite outcome were similar between the intervention group and control group (RR = 1.00, 95% CI 0.85-1.19, p = 0.961).

As shown in Figure 6, in the rural areas the incidence rates of completed suicides were similar between the intervention group and control group (RR = 1.09, 95% CI 0.82–1.45, p = 0.550). A subgroup analysis demonstrated that the incidence rates in the intervention group were higher in females (RR = 1.44, 95% CI 0.85–2.43, p = 0.177).

As shown in Figure 7, in the rural areas, the incidence rates of suicide attempts requiring admission to an emergency ward for critical care in the intervention group were slightly lower than those obtained from the control group (RR = 0.86, 95% CI 0.55–1.36, p=0.524). A subgroup analysis demonstrated that the incidence rates in the intervention group were significantly lower in males (RR = 0.39, 95% CI 0.22–0.68, p=0.001) and the elderly over 65 years old (RR = 0.35, 95% CI 0.17–0.71, p=0.004). The subgroup analysis demonstrated that the incidence rates in the intervention group were lower in participants younger than 25 years old (RR = 0.74, 95% CI 0.24–2.31, p=0.605), while the incidence rates were higher in females (RR = 1.56, 95% CI 0.80–3.04, p=0.193).

Table 2. Population characteristics at baseline (2006.1-6) in rural and highly populated areas N (%).

	Group 1		Group2	
	(Rural areas)		(Highly populated a	reas)
	Intervention	Control	Intervention	Control
	n=7	n = 10	n=3	n=3
All	291,459	339,674	615,586	704,341
Sex				
Male	136,399 (47)	159,380 (47)	310,301 (50)	348,153 (49)
Female	155,060 (53)	180,294 (53)	305,285 (50)	356,188 (51)
Age				
under 25	47,892 (16)	52,867 (16)	103,218 (17)	119,512 (17)
25–64	157,887 (55)	181,153 (53)	407,801 (66)	448,270 (64)
65 and over	85,680 (29)	105,654 (31)	104,567 (17)	136,559 (19)
Region				
Aomori	35,668 (12)	60,695 (18)	-	-
Akita	59,237 (20)	66,678 (20)	-	-
lwate	55,416 (19)	61,589 (18)	-	-
Minami-Kyushu	141,138 (48)	150,712 (44)	-	-
Sendai	-	-	160,368 (26)	197,915 (28)
Chiba	-	-	411,025 (67)	425,177 (60)
Kita-Kyushu	_	_	44,193 (7)	81,259 (12)

doi:10.1371/journal.pone.0074902.t002

		Intervention	ıtion						Control						
		Combined	pa	Completed suicide	ted	Suicide attempt		Population	Combined	pa	Completed suicide	pa	Suicide attempt	. +	Population
		z	Rate	z	Rate	z	Rate	z	z	Rate	z	Rate	z	Rate	z
Before	2003.1-6	128	86.1	89	45.7	09	40.4	297,397	131	75.3	77	44.2	54	31.0	348,092
	2003. 7-12	91	61.4	89	45.9	23	15.5	296,447	95	54.8	74	42.7	21	12.1	346,639
	2004.1-6	126	85.2	105	71.0	21	14.2	295,655	94	54.4	69	40.0	25	14.5	345,415
	2004. 7-12	70	47.5	49	33.3	21	14.3	294,665	122	71.0	73	42.5	49	28.5	343,825
	2005.1-6	77	52.5	57	38.8	20	13.6	293,589	80	46.7	99	32.7	24	14.0	342,382
	2005. 7-12	102	8.69	51	34.9	51	34.9	292,467	138	81.0	69	40.5	69	40.5	340,927
Reference	2006. 1-6	91	62.4	62	42.5	29	19.9	291,459	139	81.8	92	44.7	63	37.1	339,674
Study	2006. 7-12	86	9.79	72	49.6	26	17.9	290,122	68	52.7	57	33.8	32	19.0	337,668
period	2007. 1-6	68	61.6	95	38.8	33	22.8	288,882	103	61.3	62	36.9	41	24.4	335,894
	2007. 6-12	99	45.9	41	28.5	25	17.4	287,276	103	61.8	57	34.2	46	27.6	333,409
	2008. 1-6	73	51.1	49	34.3	24	16.8	285,773	92	55.6	09	36.2	32	19.3	331,133
	2008. 7-12	71	49.9	44	30.9	27	19.0	284,379	128	77.8	80	48.6	48	29.2	328,951
	2009. 1-6	93	65.7	19	43.1	32	22.6	283,090	06	55.0	61	37.3	59	17.7	326,977
	2009. 6-12	72	51.1	54	38.3	18	12.8	281,763	114	70.1	70	43.1	4	27.1	325,146

Combined: Completed suicide and suicide attempt. Rate: per 10,000 persons, per year. doi:10.1371/journal.pone.0074902.t003

Table 3.

Table 4.

Highly pop	ulated areas														
		Inter	ventio	n					Cont	rol					
		Com	bined	Con	npleted ide	Suici atter		Population	Coml	bined	Com suici	pleted ide	Suici atten		Population
		N	Rate	N	Rate	N	Rate	N	N	Rate	N	Rate	N	Rate	N
Before	2003.1-6	147	48.3	71	23.3	76	25.0	608,545	176	50.2	99	28.3	77	22.0	700,674
	2003. 7-12	154	50.5	74	24.3	80	26.2	609,571	212	60.5	101	28.8	111	31.7	701,360
	2004.1-6	134	43.9	66	21.6	68	22.3	610,644	168	47.9	79	22.5	89	25.4	702,094
	2004. 7-12	136	44.5	70	22.9	66	21.6	611,912	171	48.7	84	23.9	87	24.8	702,467
	2005.1-6	160	52.2	75	24.5	85	27.7	613,223	199	56.6	94	26.7	105	29.9	702,882
	2005. 7-12	122	39.7	61	19.9	61	19.9	614,385	174	49.5	87	24.7	87	24.7	703,589
Reference	2006. 1-6	166	53.9	70	22.7	96	31.2	615,586	197	55.9	97	27.5	100	28.4	704,341
Study	2006. 7-12	202	65.5	80	25.9	122	39.5	617,137	208	59.0	83	23.5	125	35.5	705,159
period	2007. 1-6	164	53.0	68	22.0	96	31.0	618,734	208	58.9	89	25.2	119	33.7	706,016
	2007. 6-12	154	49.6	74	23.8	80	25.8	620,562	190	53.7	91	25.7	99	28.0	707,088
	2008. 1-6	148	47.6	81	26.0	67	21.5	622,435	202	57.0	89	25.1	113	31.9	708,205
	2008. 7-12	165	52.9	67	21.5	95	30.4	624,319	222	62.6	87	24.5	135	38.0	709,661
	2009. 1-6	156	49.8	80	25.5	76	24.3	626,250	190	53.4	86	24.2	104	29.2	711,167

Combined: Completed suicide and suicide attempt.

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Rate: per 10000 persons, per year.

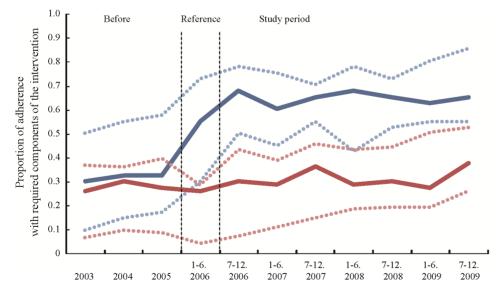
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As shown in Figure 6 and 7, in the highly populated areas, the RRs of suicide attempts and completed suicide demonstrated heterogeneous effects.

Discussion

In the present study, the intervention had unclear effects on the overall rate ratio of the composite outcome in rural areas where the suicide rate was high. The overall rate ratio of the composite outcome in the intervention group was 7% lower than that obtained from the control group. This was possibly because the intervention had some heterogeneous effects on different subpopulations. Indeed, the RR in males was significantly lower. It was also demonstrated that the RR in the elderly was lower, while it was higher in females and in younger participants. Interestingly, our secondary analysis suggested that the effects were more



86

27.4

626,963

208

58.4

92

25.8

116

32.6

711,837

Figure 3. Figure 3 shows the proportion of adherence with required components of the intervention in the rural areas. The blue line indicates the proportion of the intervention group, and the red line indicates that of the control group. The dotted lines indicate interquartile ranges. The proportion is shown from the 3.5 years before the start of the study period. The six-month period before the start of the study period was the reference period.

doi:10.1371/journal.pone.0074902.g003

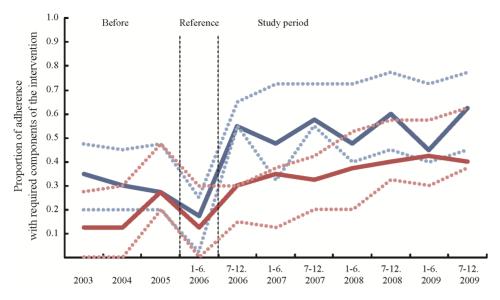
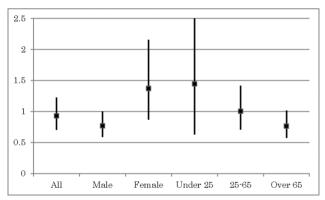


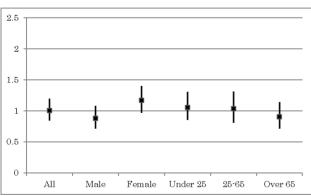
Figure 4. Figure 4 shows the proportion of adherence with required components of the intervention in the highly populated areas. The blue line indicates the proportion of the intervention group, and the red line indicates that of the control group. The dotted lines indicate interquartile ranges. The proportion is shown from the 3.5 years before the start of the study period. The six-month period before the start of the study period was the reference period. doi:10.1371/journal.pone.0074902.q004

Primary outcome at all and subgroups (sex and age) in Group1



■ Rate Ratio, - 95%CI

Primary outcome at all and subgroups (sex and age) in Group 2



■ Rate Ratio, - 95%CI

Figure 5. Primary outcome (composite outcome, consisting of completed suicides and suicide attempts requiring admission to an emergency ward for critical care) for all and for subgroups (sex and age) in rural areas and in highly populated areas.

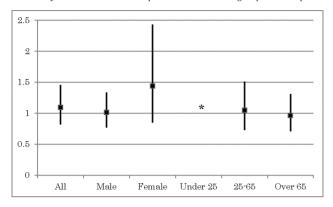
doi:10.1371/journal.pone.0074902.g005

apparent in the incidence of suicide attempts than that of completed suicides. It was demonstrated that the RR of suicide attempts in the intervention group was significantly lower in males and in the elderly. Thus, this study apparently demonstrated the heterogeneous effects of the intervention on the different subpopulations.

The beneficial effect of the intervention in males is consistent with a previous report showing a significant reduction of suicide rate through a community-based intervention in the US Air Force, in which about 84% of participants were males. 15 Interventions used in the study aimed to establish a seamless system of services across multidisciplinary human services with very strong and vertical leadership involvement. From another point of view, it is well known that about 90% of suicides are associated with mental illness, i.e., depression and other affective disorders, schizophrenia, substance/alcohol-related disorders and personality disorders. [16,17] The interventions in the US Air Force study covered not only depression but also a range of psychosocial risk factors for suicide, and thus were multilevel and multimodal. Although the sample size was quite large, the US Air Force study was a quasiexperimental pre-post design conducted in a single organisation (Table 5). In the present study, we conducted a parallel comparative trial in multiple regions to examine the effectiveness of a similar approach. Therefore, our study has reproduced and extended the findings of the US Air Force study. Here, it is concluded that a community-based multimodal intervention would be recommended for males. It is still unclear which component of the complex intervention programs is especially important for males.

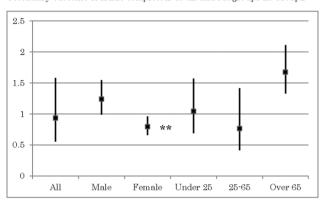
In this study, we developed our intervention by extending the findings from previous studies, focusing especially on elderly. [5–7] As we expected, beneficial effects of the intervention in the elderly were consistent with these previous observations. [5–7] In their interventions, psychiatrists and public health nurses tried to reinforce human relationships and connectedness in their community by home visiting and regional social gatherings. However, these previous studies were retrospective pre-post designs with one or a few communities. Therefore, our study confirmed the findings

Secondary outcome (Suicide completed) at all and subgroups in Group1



- Rate Ratio, 95%CI
- * Not calculated

Secondary outcome (Suicide completed) at all and subgroups in Group2



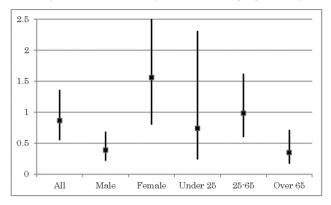
- Rate Ratio, 95%CI
- ** Interaction (intervention × year) was significant, p= 0.0270

Figure 6. Secondary outcome (completed suicides) for all and for subgroups in rural areas and in highly populated areas. doi:10.1371/journal.pone.0074902.g006

for elderly and concluded that the effect would be significant in this group.

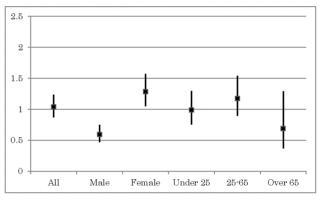
As shown in Table 5, there are some reports of multilevel interventions focusing on depression care. [18,19] These interventions aimed to introduce untreated depressed patients to appropriate care by public awareness campaigns, educating general practitioners and supporting them with mental health professionals, and encouraging collaborative care. A German study, the Nuremberg Alliance Against Depression, reported a reduction in nonfatal suicide attempts in an intervention region compared with a control region but no difference in effect on the rate of completed suicides. [18] In the report from Hungary, the rate of completed suicides in the intervention region was not different from that in the control region. [19] Although the type of our intervention was different from these two studies, the absence of the effect on the rate of completed suicides in the intervention region was also observed in our NOCOMIT-J. On the contrary, as described above, the US Air Force study, which covered various risk factors, showed a significant reduction of the rate of completed suicides. [15] A high rate of adherence to the intervention (over 80%) might help to achieve the objective of lowering completed suicide rates (Table 5).

Secondary outcome (Suicide attempted) at all and subgroups in Group1



■ Rate Ratio, - 95%CI

Secondary outcome (Suicide attempted) at all and subgroups in Group 2



■ Rate Ratio, - 95%CI

Figure 7. Secondary outcome (suicide attempts) for all and for subgroups in rural areas and in highly populated areas. doi:10.1371/journal.pone.0074902.g007

The incidences of suicidal behaviour were similar between the intervention group and control group in the highly populated areas near metropolitan cities, not unexpected as adherence of the intervention group to the suicide prevention programs was not different from that of the control group. In addition, adherence of the intervention group in highly populated area was relatively low, suggesting the difficulties of implementing the intervention in these areas. Further improvement of the intervention programs would be necessary to make the intervention feasible in the highly populated areas.

There are several limitations of the present study. 1) The study was not a randomised trial. Therefore, we used a matched pair design and a model adjusted for possible confounding factors in the analysis. However, some unmeasured and residual confounders may still persist. We need to perform randomised trials confirming our insights. 2) The study participants, investigators and the reporters of events were not blind to the intervention. Although the outcomes were systematically collected from official records, the study might have some misclassification bias. 3) Adherence to the intervention was limited. The adherence would be improved by investing sufficient budgets and resources.

In conclusion, our findings suggest that the community-based multimodal intervention for suicide could be implemented in the all areas. However, the effectiveness of the intervention are shown

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	Results	Significant 33% reduction of suicide (RR 0.67, 0.57–0.80) compared to control	19.4% to 24% reduction suicide acts rate (p = 0.082, 0.004) compared to control			No significant difference between intervention and control overall, but female suicide decreased by 34% in intervention and increased by 90% in control; significant decrease compared to county and country (Hungary) levels.			9% reduction, not significant, but men 23% (p = 0.0485), over 62 24%(p = 0.062) reduction compared to concurrent control
	Analysis	χ2 test for linear trend with the Mantel- Haenszel, and relative-risk (RR),(No adjustment for sex and age)	Change rate and χ^2 test (stratified sex and years, but not adjusted)			Poisson log-link function, Mixed linear models with repeated measures (adjusted years, stratified sex, but not adjusted age)			Poisson log-link function, Marginal models in repeated measures with GEE (adjusted sex, age and years)
	Outcome	Completed suicides, homicide, accidental death,?family?violence	Completed suicide, suicide attempted, And combined (suicide acts)			Completed suicides (from police), prescription of anti-depressants, alcohol related death and unemployment			Completed suicides from government), suicide attempts, and combined
	Compliance	Over 80%	Unknown percentage (details of activities only)			About 60% (39–90%)			About 70% in rural areas, About 55% in highly populated areas
	Duration	5 years	2 years			5 years			3.5 years
	Pre suicide rate	1990–6 (median 13.1)	Intervention (about 18) vs. control (about 15)			Intervention (median 57.5) vs. control (median 56)			Intervention (median 42.5) vs. control (median 42.5) in rural areas
	Intervention	Multimodal (10 initiatives)	sed) 4 levels; Training of primary care physicians, public ty) campaign for depression, corporation with facilitators and self-help activities support			(Non-randomised) Training of primary concurrent care physicians and comparative nurse, plus tele-(a region vs. a phone psychiatrist region) design consultation			Multimodal (4 levels)
	Study Design	nental) st design	(Non-randomised) concurrent comparative (a city vs. a city) design						(Non-randomised) controlled (matched) concurrent comparative (2 areas and 4 regions) design
	Sex, Age	About 84% men (Quasi- experir pre-po	No data (no differences between pre-post)	0		48% were men, 22% were over age 60	ر		47% were men, 30% were 65 over aged
	Study Size, Sites	5,260,292	720,000	Intervention: Nuremberg, 480,000 Control: Wurzburg	270,000	a 127,000	Intervention: Kiskunhalas,73,000 (44,000 in villages and 29,000 in a town) with 28 GPs	Control: Bacs- Kuskun,54,000 (22,000 in villages and 32,000 in a town)	631,133 (rural area)
	Population	US Air Force personnel	Inhabitants living in the city			A region with a 127,000 igh suicide rate in Hungary			Inhabitants living in high suicide-rate areas in Japan
	Study	Knox et al., BMJ. US Air Force 2003 Dec 13; personnel 327(7428):1376.	Hegerl et al., Psychol Med. 2006; 36(9): 1225–33.			Szanto et al., A region with a Arch Gen igh suicide rate Psychiatry. 2007; in Hungary 64(8): 914–20.			NOCOMIT-J
C	NE w	ww.plosone.org				10	October 2013	Volume 8	Issue 10 e74902

Study	Population Study		Size, Sites Sex, Age	Study Design Intervention	Intervention	Pre suicide rate Duration Compliance Outcome	Duration	Compliance	Outcome	
		7 intervention vs. 10 control	0							
		1,319,927 (highly populated area)				Intervention (median 22.9) vs. control (median 26.7)	-			
1						in highly populate areas	p			
		4 interventions vs. 4 controls	4							

for males and for the elderly in rural area. Therefore, it would be recommended for males and for the elderly in rural areas.

Acknowledgments

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deepest sorrow for the loss of Dr. Toshiharu Fujita, who greatly contributed to the design of this trial.

Author Contributions

Conceived and designed the experiments: YO AS NI HS NY. Performed the experiments: KO HU SA YI HI YK YM JN NN NW TY AN YS MT ET. Analyzed the data: NI HS NY. Contributed reagents/materials/ analysis tools: KO HU HO. Wrote the paper: YO AS NY.

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