Abstract

Background: This systematic review provided evidence for the Canadian Task Force on Preventive Health Care to update their guideline regarding screening for depression in adults at average or high risk for depression.

Methods: Six databases were searched from 1994 to May 2012 for randomized controlled trials, observational studies, and systematic reviews on the benefits or harms of screening. Relevance screening, data extraction, risk of bias analyses, and quality assessments were completed in duplicate. A meta-analysis was conducted using the generic inverse variance method

Results: Five cluster controlled studies were included that reported on the effect of community-based depression screening (CDS) with follow-up on the completed suicide risk for elderly residents in rural Japan. The CDS program had a protective effect on the overall incidence of completed suicide (RRR 0.5, 95% CI, 0.32 to 0.78; p=0.002) which was demonstrated for women (RRR=0.37 95% CI, 0.21 to 0.67; p=0.0006), but not men (RRR=0.67, 95% CI, 0.35 to 1.27; p=0.22). No studies met the inclusion criteria concerning harms of screening.

Conclusions: The ultimate goal of screening for depression is to decrease incidence of and mortality from this disease. Limited evidence allows conclusions regarding the effectiveness of screening in general or high risk populations.

Introduction

Depression is a complex mental illness that is associated with disability and reduced quality of life for the person with the disorder, as well as posing a substantial societal burden. Prevalence of depression in the Canadian population has been estimated to vary from 5 to 8.2 percent annually.[1,2] The systematic review on which this paper is based provided evidence for the Canadian Task Force on Preventive Health Care (CTFPHC) to update their guideline regarding screening of adults (at average or high risk for depression) 18 years and older for depression.[3] The WHO Psychological Problems in General Health Care study[4] released in 1996, reported that primary care physicians diagnosed only 42 percent of adult patients with major depression. Potential benefits of screening for depression in adults include improved detection of major depression disorder (MDD), dysthymia, and subsyndromal depression which can lead to earlier treatment. Treatment of MDD in adults is thought to result in improved outcomes such as quality of life, work life, and minimized risk of suicide.[5] This review was designed to determine which of these benefits are supported by evidence.

One argument against screening is that in up to 50 percent of people depression resolves without treatment within 3 months.[6] In addition, screening instruments have a low positive predictive value, meaning that many who screen positive do not have depression.[7,8]Although a previous review found no literature specifically evaluating harms associated with screening for depression and related disorders,[9] those persons screening positive for depression who do not have the disorder may be exposed to stigmatization, further psychological testing, as well as unnecessary psychological and pharmacological treatment regimes. This systematic review explores the benefits and harms of screening for depression in: a) asymptomatic adults 18 years of age or over from the general population, and b) adults at high risk for depression, in (i) primary care or (ii) other outpatient settings.

Methods

The search strategy was developed by a librarian experienced in searches for systematic reviews. Several electronic databases were searched: Medline, EMBASE, PsycINFO, Cochrane Central and Cochrane Database of Systematic Reviews from 1994 to May 23, 2012. The search was broad with the only limitations being date, human subjects and English or French language. In addition, a grey literature search was undertaken focusing on Canadian sources using a number of keyword terms for depression and screening.

Eligible studies included adults ≥18 from unselected populations or high risk groups. The intervention of interest was routine screening as a normal part of care and any comparative study design with a screen versus no-screen comparison.

Study selection and data extraction

Pairs of reviewers independently screened all identified citations for relevance, inclusion, quality and data extraction. Conflicts were resolved through discussion. Any citation deemed potentially relevant was retrieved for full review. Reference lists of on-topic systematic reviews were searched to ensure all primary studies meeting our inclusion criteria were considered. The study settings were primary care or, of high risk groups, specialty clinics.

Quality assessment

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) system was used to determine quality of the evidence. GRADE considers five criteria (design, consistency, directness, precision, reporting bias) to rate the quality of evidence as high, moderate, low or very low, indicating the assessment of the likelihood that further research

will impact the estimate of effect.[10] After two reviewers independently assessed the evidence on these criteria, agreement between the ratings and the overall quality of the summary statistics was reached.

Statistical analysis

Data were presented in the papers as pre (baseline) and post (implementation) analysis for both intervention and control groups. Two of the five identified papers[11,12] included two control groups; the remaining three had one control group. Four out of the five papers presented data using adjusted incidence rate ratios (IRR) and one reported adjusted odds ratios. This required we to calculate the ratio of rate ratios (RRR) for each group. Ratio of rate ratios is the ratio of the post- to pre-rate ratio in the intervention area divided by the corresponding post- to pre-rate ratio in the control area.

A weighted intervention effect was calculated across studies using data for overall population and stratified for age and gender. A RRR of less than 1.0 shows the reduction in the suicide IRR in the intervention area to that predicted from the IRR in the control area, assuming that any changes to the population at risk in the intervention area are the same as those in the control area. Standard errors for logarithms of rate ratios and 95% CIs for rate ratios were calculated assuming that the number of events in each area in each period followed a Poisson distribution. The generic inverse variance method was used with a random effects meta-analysis model, since all studies were done by the same team/authors working the same research design. The Cochrane's Q (α=0.10) and I^2 statistic were employed to quantify the statistical heterogeneity between studies, where $p<0.10$ indicates a high level of statistical heterogenity between studies.[13]

Results

Study selection and characteristics

Figure 1 shows the selection of studies. Our search located 14,226 potentially relevant citations. At title and abstract screening, 12,694 were excluded. A total of 1,532 papers were retrieved and were assessed on inclusion criteria. Of those 1,527 papers did not meet our inclusion critieria. The five included studies had the same first author.

The first question was: "What is the evidence for the benefit of screening for depression in: a) asymptomatic adults 18 years of age or over from the general population (i) primary care or (ii) other outpatient settings to improve critical outcomes?". No studies of screening for the depression in the general population as a whole met the inclusion criteria of this review. Five primary studies with community depression screening in the elderly met the inclusion criteria and provide the evidence for the review questions. These studies were conducted in rural regions of Japan with suicide rates in the elderly ranging from 49.6 to 418.4/100,000 in women and 113 to 326/100,000 in men,[11,12,14-16] and targeted the residents aged 60 and over. Oyama et al., (1978 to 2006)[11,12,14-16] developed a universal suicide prevention program, which included a screening component adapted from the WHO World Mental Health Survey.[17] This involved screening for depression, follow-up with mental health care or psychiatric treatment, and psychoeducation in the community setting. The duration of studies varied from 4 to 20 years. The overall aim of these studies was to evaluate the effectiveness of the community-based depression screening (CDS) program in both the short- and long-term.

All five studies used a pre- and post-implementation design, with an intervention community and a control community with similar demographics. In all studies, more than 60 percent of men and more

than 80 percent of women in the targeted residents (aged ≥60) participated in the program during the implementation.

The five studies implemented similar programs, providing a two-step screening and follow-up process for depression. In the first step, the older residents of the selected communities were called to participate in an educational health workshop on the signs and possible treatments for depression and suicide risk and also on how to use mental health services. Following the workshop, those who agreed to participate in the program completed the Japanese version of the Self-rating Depression Scale (SDS),[18] or the Geriatric Depression Scale five-item (GDS-5).[19] Those who did not attend the workshop were contacted the following day and asked to participate in the program. Examiners then visited those who agreed to participate, and conducted the program following the same procedures. There were several examiners, including psychiatrists and public health nurses (PHNs).

In the second step, a mental health assessment was carried out by a PHN on enrolled participants with positive screening results on the SDS. Japanese translated schedules of a standardized assessment of patients with depressive disorders were used[20,21] and a clinical decision was made about whether a psychiatrist's medical examination was necessary. Throughout the interview, if the participants were suspected of having depression, they were given a clinical decision as to whether to refer to a psychiatrist or to continue to the PHN's follow-up interview, and were then re-examined.

The meta-analysis of the target population involved 70,053 person-years and 65 suicide victims in intervention groups compared to 113,324 person-years and 145 suicide victims in the control groups during the implementation period. These studies reported six gender- and age-specific target population groups (age group 65 to 74, 75 to 84, and ≥85), with the exception of one

study[16] that had different age groups (60 to 69, 70 to 79, ≥80). All five studies provided sufficient data stratified by age, gender, and time periods for baseline and program implementation.

All the studies[11,12,14-16] demonstrated a statistically significant reduction in the number of completed suicides after implementation of the CDS program (RRR=0.5, 95% CI, 0.32 to 0.78; p=0.002). There was no significant heterogeneity among these studies (I^2=21%, χ^2=5.04; p=0.28). The outcome measure was an IRR based on binary data (i.e., suicide/no suicide that was calculated in both implementation and control before and after the intervention). There was no significant heterogeneity among these studies in either men or women, (I^2=21%, χ^2=5.07; p=0.28) and (I^2=0%, χ^2=1.41; p=0.84), respectively. Publication bias could not be assessed given the small number of included studies.

The difference between pooled incidence rate ratios and the corresponding 95% CI for completed suicide were calculated using the generic inverse variance weighting method for total number of men and women. The RRR of the data from all five included studies[11,12,14-16] suggested that the CDS program had a protective effect on the overall IRR (RRR=0.50, 95% CI, 0.32 to 0.78; p=0.002) (Figure 3) . The RRR also showed reduction in suicide of women (RRR=0.37, 95% CI, 0.21 to 0.66; p=0.0006), whereas in men the effect was not significant (RRR=0.67, 95% CI, 0.35 to 1.27; p=0.22) (Figure 2).

Subgroup analysis

We considered subgroup analysis based on population characteristics. We carried out prespecified subgroup analyses by age groups (65-74, 75-84, and 85 or older) (Figure 4) and by gender and age groups (i.e men and women in age groups 65-74, 75-84, and 85 or older).

Data were pooled from the five studies reporting suicide rates for subgroups of similar age groups. As outlined above, four out of the five studies had similar age groups[11,12,14,15] and the other had a slightly different age group.[16]

To compare pooled results from all five of the studies with the pooled results of only the four studies with the same age groups, we carried out two separate pooled analyses. We did not find significant differences between the two analyses in terms of heterogeneity in all age groups in both men and women. We calculated the RRR for pre- and post-data in both the intervention and control groups for each specific age group and by gender and specific age group from the data in each study. Outcomes of individual studies and a summary of meta-analyses results for each age group and for each age group in both women and men are shown in Figures 5-6. Meta-analysis stratified by age groups showed a significant reduction effect on suicide in elderly at ages between 65 to 74 years (RRR=0.49, 95% CI, 0.26 to 0.94; p=0.03) and between 75 to 84 years (RRR=0.44, 95% CI, 0.22 to 0.88; p=0.02) (Figure 4). Subgroup meta-analysis showed a non-significant reduction effect on suicide in men across all age groups (RRR=0.74, 95% CI, 0.44 to 1.24; p=0.25) (Figure 5). There was a statistically significant reduction of completed suicide only in women at ages between 75 to 84 years (RRR=0.37, 95% CI, 0.17 to 0.81; p=0.01) (Figure 6).

GRADE Rating

According to the GRADE system for assessing quality, observational evidence (including cohort designs) begins with a LOW rating. We downgraded the evidence for indirectness given that the included studies all looked at elderly, rural Japanese populations which are unlikely to be representative of Canadians. We also downgraded the evidence because the use of community-

based depression screening (CDS) programs which incorporated education and treatment means the result cannot be attributed solely to the screening component of these programs. Thus the overall GRADE rating applied to this evidence is VERY LOW QUALITY.

High risk population

Initially, the Depression Working Group selected only the 5 high risk groups in the key questions, however it was determined that some risk groups were not represented in that list. As a result the scope of the review was extended to include any risk factor. We re-reviewed our evidence base but did not find any evidence that met our inclusion criteria for any high risk group.

Harms of Screening

No studies were identified that met the inclusion criteria of this review that addressed the harms of depression screening.

Discussion

For the question of the benefit of screening we found no direct evidence for the population as a whole, rather we have included five studies conducted by the same primary researcher in the elderly in rural Japan. Five studies met the inclusion criteria for this review; however, the results provide limited evidence on the effectiveness of screening for depression in the general population or high risk groups. We found no studies on harms of screening for depression that met our inclusion criteria. These results are consistent with previous guidelines and evidence reviews. The USPSTF 2009[9] found no evidence for the benefit of screening for depression in the absence of treatment programs. The lack of direct evidence to support general screening programs has also been recognized by NICE[22] and SIGN[23]; neither recommend screening of asymptomatic people in the general population. The NICE guideline for people with chronic

illness recommend that physicians remain alert to the possibility of depression [24] and another for perinatal women[25] recommended screening postpartum women, yet those recommendations are based on the indirect evidence of the benefit of treatment rather than the direct evidence of the effectiveness of screening or case finding for depression. The generalizability of the finding of the Oyama studies should be viewed with caution as Japan has a national suicide rate much higher than Canada or the United States. In the case of elderly women in the age group that showed benefit, the Japanese suicide rate is over 7 times higher than the Canadian rate (23.4 versus 3.3 per 100,000 respectively).[26] In addition, the regions included in the study had average rates of suicide much higher than even the Japanese average. [11,12,14-16]

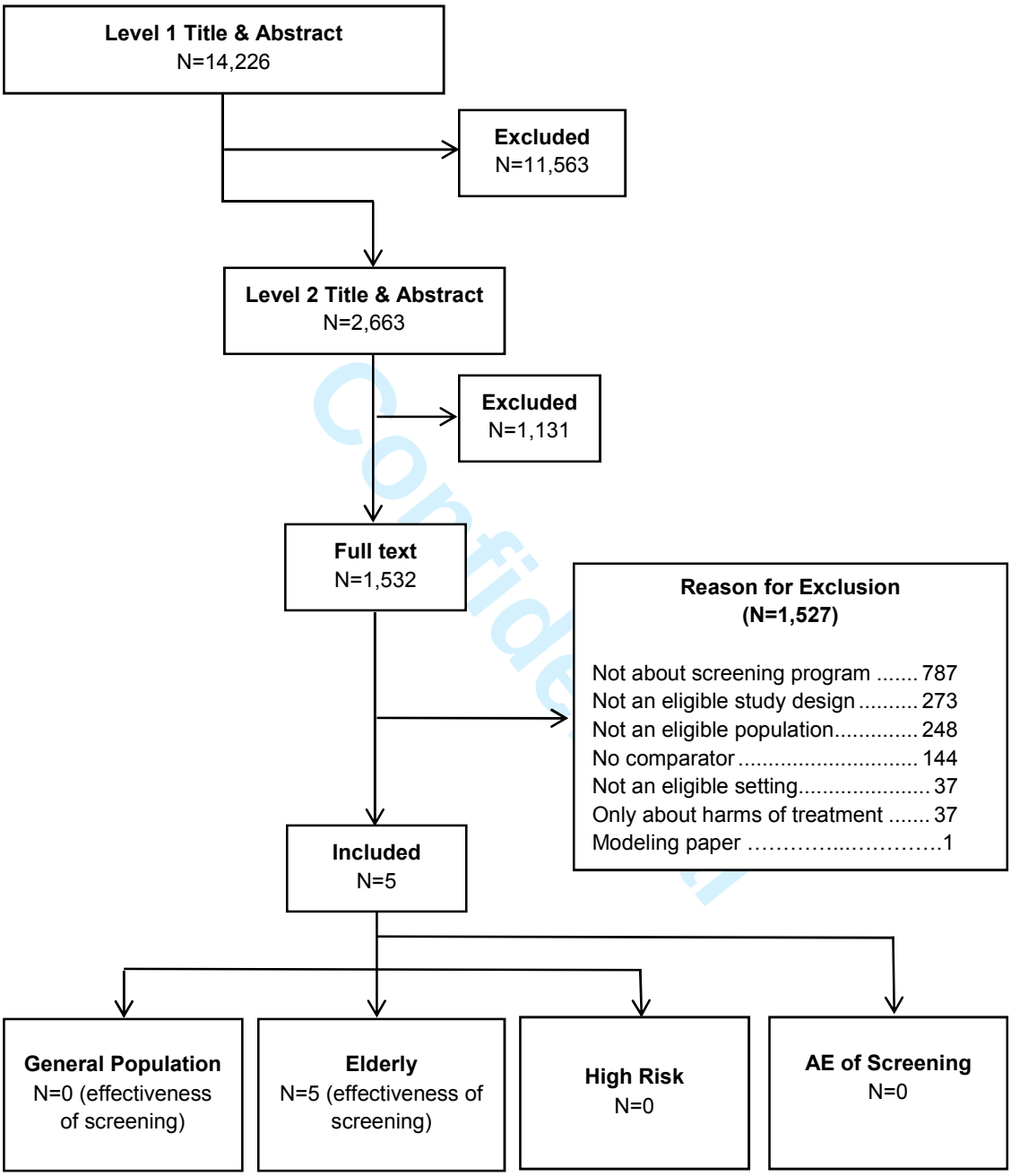
Limitations

The findings of this review are affected by the limitations of the included literature. We limited our search to papers written in English or French. There is the potential that we have missed the opportunity to analyze data from papers written in other languages. The studies that were reviewed here evaluated the effectiveness of the community-based depression screening programs which incorporated screening for depression, follow-up with mental health care or psychiatric treatment, and health education in the community setting in rural Japan with higher than average rates of suicide. As such, the observed reduction in suicide rates or recovery from depression cannot be attributed solely to the screening component of these programs.

Conclusion

The ultimate goal of screening for depression is to decrease morbidity and mortality related to this disease. There is very limited research evidence from which to draw any conclusions on the effectiveness of screening for depression in the general or high risk populations.

Figure 1. Flow of Studies to Final Number of Eligible Studies



AE=adverse events

Figure 2. Forest Plot: Effect of Community-based Suicide Prevention Program (including screening for depression) Overall Analysis

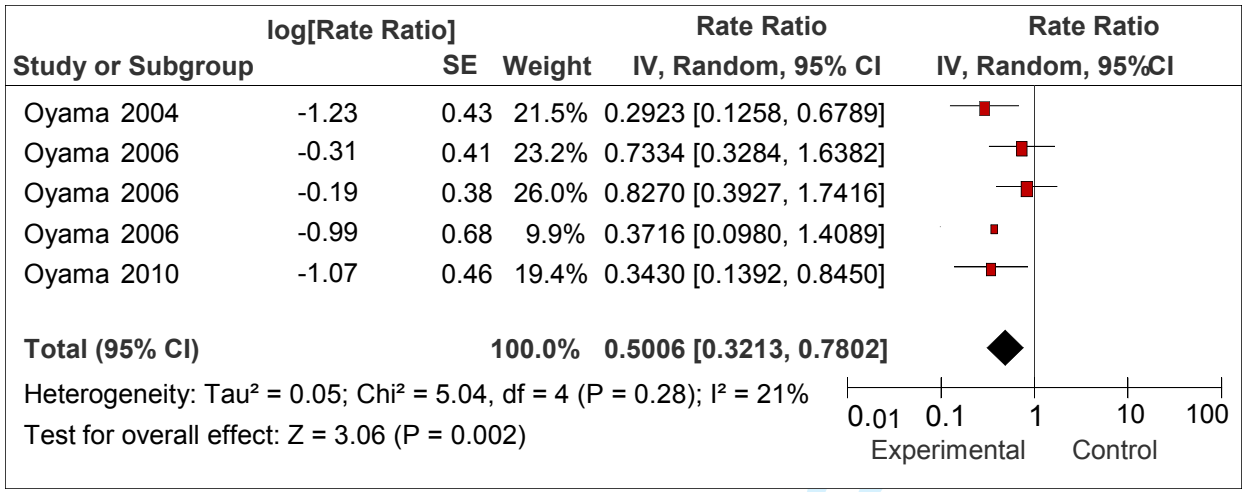


Figure 3. Forest Plot: Effect of Community-based Suicide Prevention Program (including screening for depression) on Completed Suicide by Gender

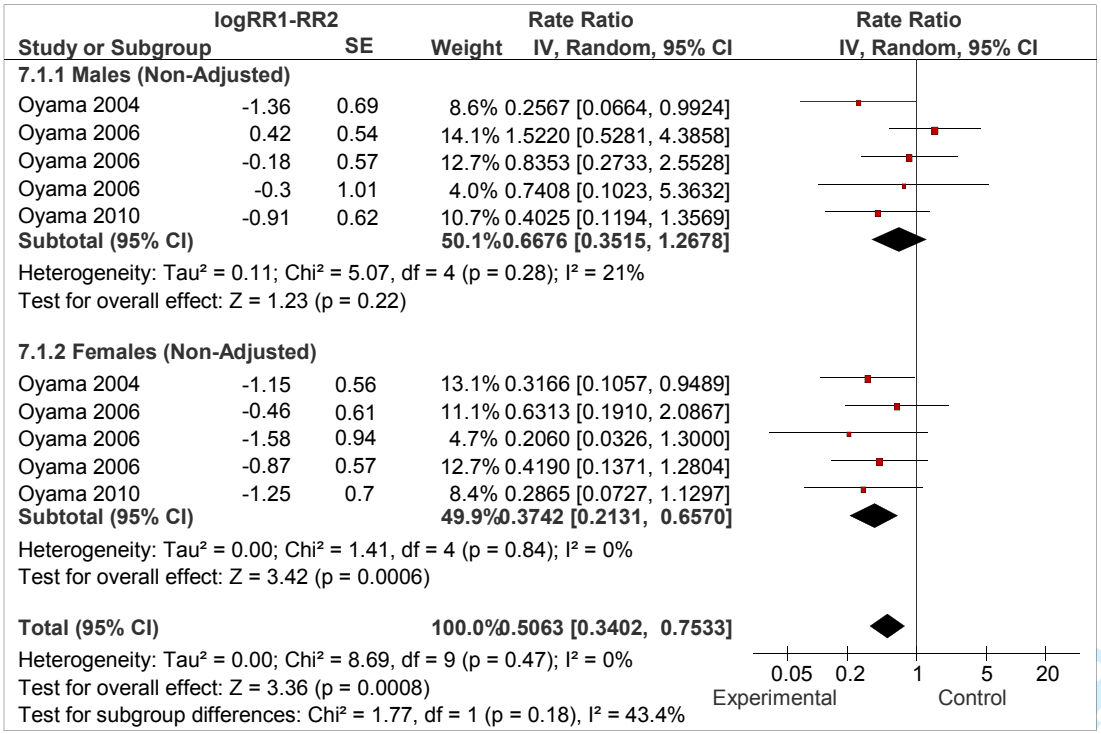


Figure 4. Forest Plot: Effect of Community-based Suicide Prevention Program (including screening for depression) by Age

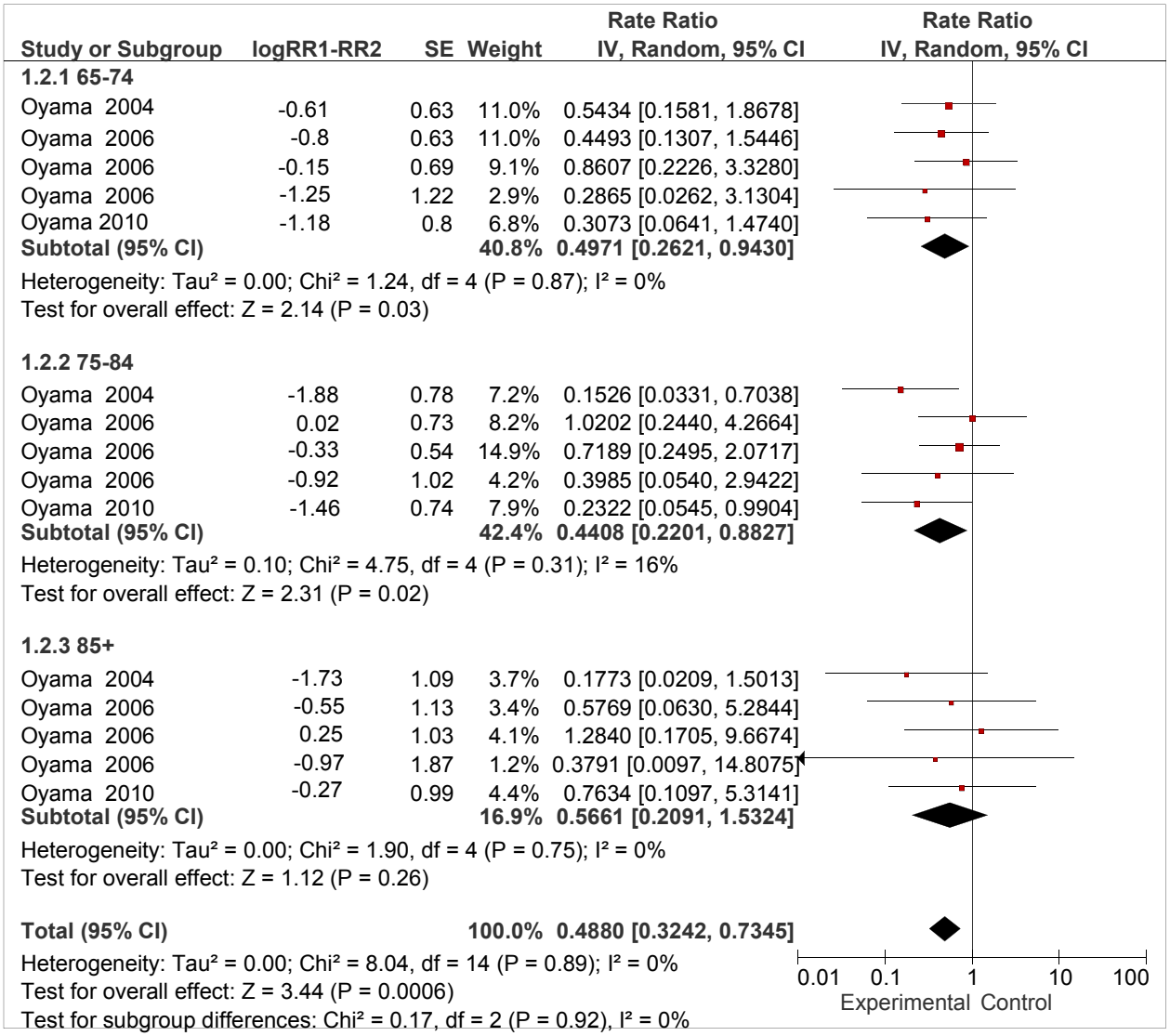


Figure 5. Forest Plot: Effect of Community-based Suicide Prevention Program (including screening for depression) by Age Group - Male

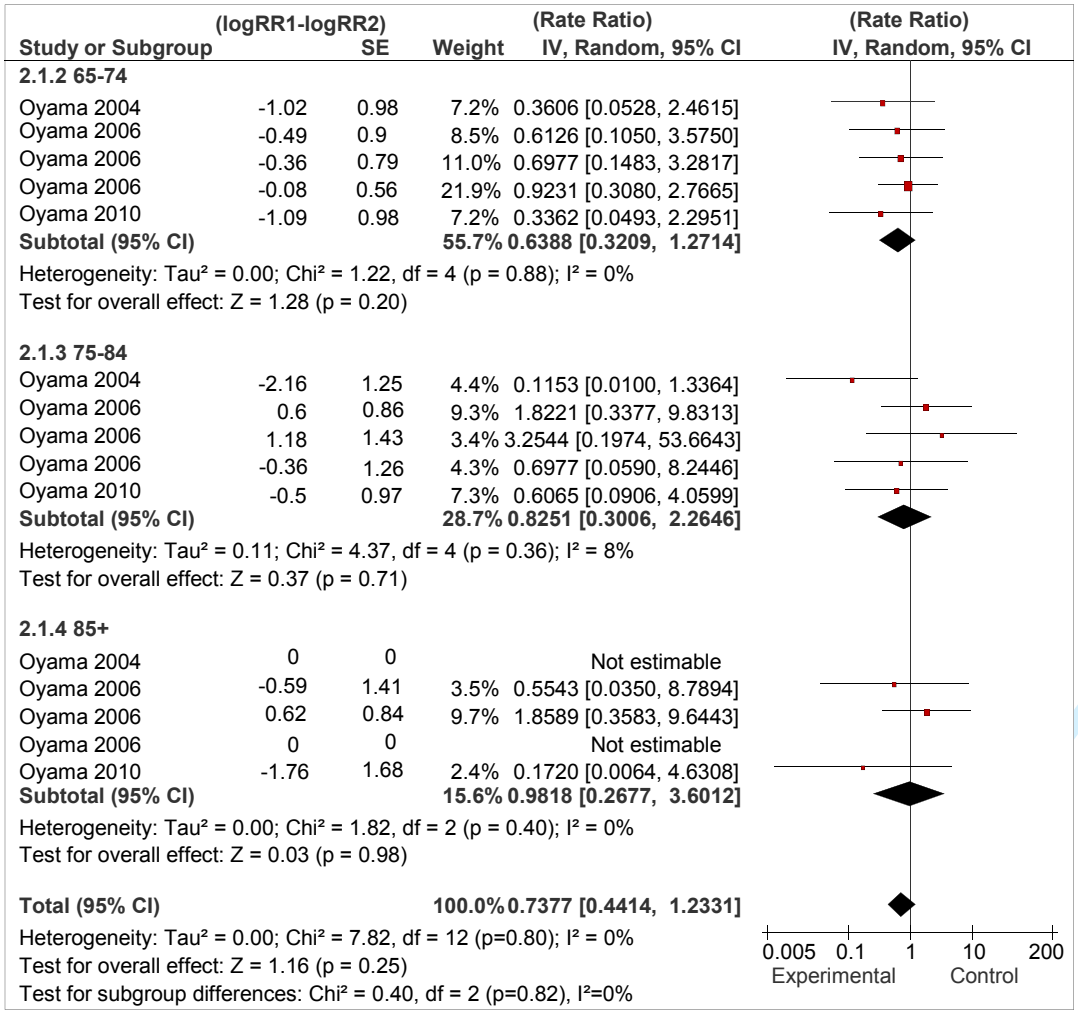
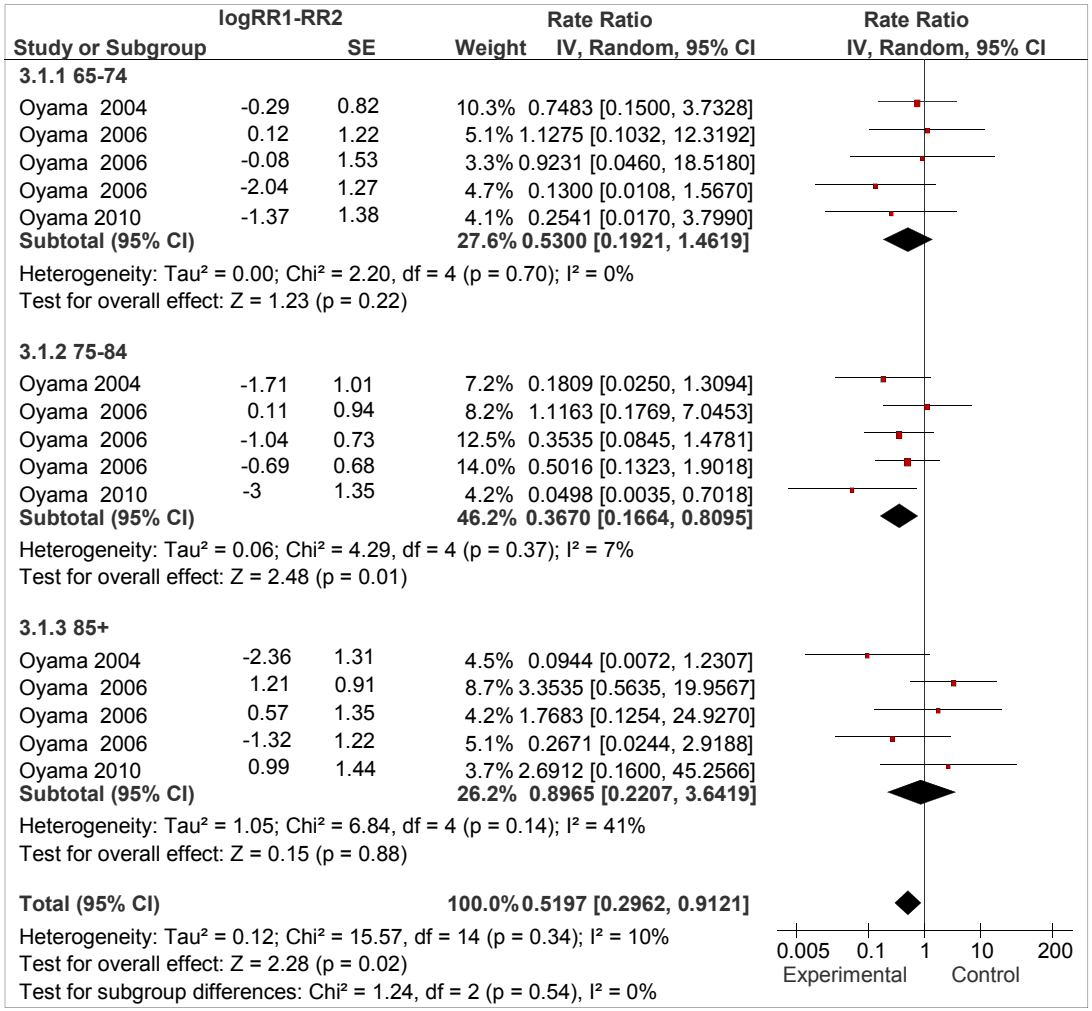


Figure 6. Forest Plot: Effect of Community-based Suicide Prevention Program (including screening for depression) by Age Group - Female



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Characteristics of Included Studies

Study	Description of Study Population	Definition of Population	Evaluation of Population	Outcomes Defined	Outcomes Descriptions
Oyama, H.[3] 2006 Design: Quasi-experimental Duration: 5 years Screening Setting: Matsudai, Japan (rural)	Intervention person years: 11,567 Control person years: 15,055 Age Mean: NR Age Range: ≥65 Age Median: NR Female: 57.6% Ethnicity: Japanese Education: NR Dx: Major and minor depression	Elderly (≥65 years old) residents living in six rural municipalities of southwest and central Japan Int: mental health workshop, referral to general practitioner or followup interview with public health nurse Exclusions: severely disabled or hospitalized cases were excluded from the study	Screening Instrument: SDS Other Rating: RDC Confirmatory Exam: ICD-9 Number of followups: 10 Number of stages: 2 ten-year	Main Outcome: Changes in suicide risk Age-adjusted IRRs of completed suicide before and after	Main Outcome: The female risk of completing suicide in the intervention area was reduced by 70%, while there was no change in the risk for males in the intervention area. Intervention: 1.02 (95% CI 0.49-2.13) in men, and 0.30 (95% CI 0.14-0.67) in women Control: No significant change
Oyama, H.[2] 2006 Design: Quasi-experimental Duration: 10 years Screening Setting: Yasuzuka, Japan (rural)	Intervention person years: 9,791 Control person years: 16,032 Age Mean: NR Age Range: ≥65 Age Median: NR Female: NR Ethnicity: Japanese Education: NR Dx: Major and minor depression	Elderly (≥65 years old) residents of an agricultural rural area in Japan with a high suicide rate Int: The intervention included (a) public health education from 1991 to 2000 and (b) screening for depression with followup from 1991 to 1997 Exclusions: NR	Screening Instrument: SDS Other Rating: RDC Confirmatory Exam: ICD-9 Number of followups: 7 Number of stages: 2 ten-year	Main Outcome: Changes in the risk of completing suicide Age-adjusted IRRs of completed suicide before and after	Main Outcome: The risk for women in the intervention area was reduced by 64% whereas there was no significant change for men in the intervention area. Intervention: 0.51 (95% CI 0.22-1.19) in men, and 0.36 (95% CI 0.14-0.93) in women Control: No significant change

Study	Description of Study Population	Definition of Population	Evaluation of Population	Outcomes Defined	Outcomes Descriptions
Oyama, H.[1] 2004 Design: Quasi-experimental Duration: 10-years Screening Setting: Joboji town, Japan (rural)	Intervention person years: 9,721 Control person years: 17,166 Age Mean: NR Age Range: ≥65 Age Median: NR Female: 50.8% Ethnicity: Japanese Education: NR Dx: Depression (unspecified)	Elderly (≥65 years old) residents of an agricultural rural area in Japan with a high suicide rate Int: Two-step depression screening performed by PHN and psychiatrist and follow-up conducted by psychiatrist every three years in targeted district of an intervention municipality, health education and emphasis on suicide taboo every year in 10-year period from 1990 Exclusions: Elderly people receiving social welfare	Screening Instrument: SDS Other Rating: SADD Confirmatory Exam: ICD-9 Number of followups: 10 Number of stages: 3 five-year	Main Outcome: Changes in suicide rates Age-adjusted IRRs of completed suicide before and after	Main Outcome: In the intervention area, a 73% reduced risk of suicidal mortality among males aged 65 and over was observed, and a 76% reduced risk of suicidal mortality among females aged 65 and over during the implementation decade, compared with the pre-implementation decade Intervention: 0.27 (95% CI 0.08-0.88) in men, and 0.24 (95% CI 0.11-0.52) in women Control: No significant change
Oyama, H.[4] 2006 Design: Quasi-experimental Duration: 5 years Screening Setting: Nagawa town, Japan (rural)	Intervention person years: 1,982 Control person years: 16,754 Age Mean: NR Age Range: ≥65 Age Median: NR Female: 59-60.8% Ethnicity: Japanese Education: NR Dx: Depression (unspecified)	Elderly (≥65 years old) residents of an agricultural rural area in Japan with a high suicide rate Int: SUPPRESS program (two-stepped screening for depression and followup by PHN, mental health workshop 3 to 4 times a year, and a group activity program once a month Exclusions: NR	Screening Instrument: SDS Other Rating: RDC Confirmatory Exam: ICD-9 Number of followups: 6 Number of stages: 2 six-year	Main Outcome: Changes in suicide risk Age-adjusted IRRs of completed suicide before and after	Main Outcome: The risk for elderly females was reduced by 74% while there was no change in the risk for males in the intervention area. Intervention: 0.48 (90% CI 0.10-2.31) in men, and 0.26 (90% CI 0.07-0.98) in women Control: No significant change

Study	Description of Study Population	Definition of Population	Evaluation of Population	Outcomes Defined	Outcomes Descriptions
Oyama, H.[5] 2010 Design: Quasi-experimental Duration: 5 years Screening Setting: Six rural municipalities of the Sanpachi Second Medical Zone, Japan (rural)	Intervention person years: 28,838 Control person years: 27,633 Age Mean: NR Age Range: ≥60 Age Median: NR Female: 57.5% Ethnicity: Japanese Education: NR Dx: Depression (unspecified)	Elderly (≥60 years) residents living in six rural municipalities of the Sanpachi Second Medical Zone (a mostly agricultural region with a high suicide rate Int: The intervention included (1) health education and (2) screening for depression with followup, using the community resources of primary care and public health nursing Exclusions: NR	Screening Instrument: CES-D, DSS Other Rating: Zung-SDS, GDS-5, CIDI Confirmatory Exam: ICD-10 Number of followups: 2 Number of stages: 2 two-year	Main Outcome: Change in the risk of completed suicide Age-adjusted IRRs of completed suicide before and after	Main Outcome: In the intervention region there was a 61% reduction in risk of suicide among men aged 60 and over. The 51% reduction in risk in women aged 60 and over did not reach statistical significance. Intervention: 0.39 (90% CI 0.18-0.87) in men, and 0.49 (90% CI 0.19-1.22) in women Control: No significant change

Abbreviations: CES-D = Center for Epidemiologic Studies Depression Scale; CI = confidence interval; CIDI = Composite International Diagnostic Interview; DSS = Depression and Suicide Screen; DX = diagnosis; GDS-5 = Geriatric Depression Scale of five items; ICD = International Statistical Classification of Diseases; Int = Intervention; IRR = incidence rate ratio; NR = not reported; PHN = public health nurse; RDC = Research Diagnostic Criteria; SADD = Schedules of Standardized Assessment of Patient with Depressive Disorders**;** Zung-SDS = Zung Self-Rating Depression Scale

PRISMA 2009 Checklist

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

PRISMA 2009 Checklist

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

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

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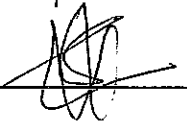

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