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Masterarbeit

# Meta-Analysis of brief contact interventions to prevent suicide reattempts

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#### Abstract

**Background:** Globally, 800,000 people die by suicide every year. Brief contact interventions are time efficient and low-cost intervention to prevent suicide reattempts. This review aims to assess the efficacy of brief contact interventions compared to control interventions.

**Methods:** This is a systematic review and meta-analysis. MEDLINE, Embase, and references of other systematic reviews were searched for randomised controlled trials comparing brief contact interventions with control interventions in patients with a recent suicide attempt. The primary outcomes were suicides and suicide attempts. The quality of evidence was assessed using Risk of Bias and Grading Recommendations Assessment Development Evaluation.

**Results:** A total of 16 trials randomising 8960 participants were included. All results were at high risk of bias and the certainty of evidence was very low. Meta-analysis showed no evidence of a beneficial effect on suicides from brief contact interventions compared to control interventions (risk ratio (RR) 0.46; 95% CI 0.22 to 0.97; p < 0.04; 8 trials). Meta-analysis showed no evidence of a beneficial effect on suicide attempts compared to control interventions (risk ratio (RR) 0.87; 95% CI 0.72 to 1.05; p < 0.14; 13 trials).

**Conclusion:** The brief intervention and contact program by the World Health Organisation seems to be most effective, though this is still based on preliminary evidence.

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# List of abbreviations

BCI	Brief Contact Intervention
BIC-program	Brief Intervention and Contact program
GRADE	Grading Recommendations Assessment Development Evaluation
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis

#### **1** Introduction

#### 1.1 Description of the suicide condition

Globally, over 800,000 people die by suicide annually, with more women attempting and more men completing suicide (Henderson et al., 2005; Schrijvers et al., 2012; Tsirigotis et al., 2011; World Health Organization, 2014). When divided by age group 0.6 to 24.5 out of 100.000 people died by suicide globally in 2019 (Global Burden of Disease Collaborative Network, 2019), though suicide differs between countries (World Health Organization, 2014). Suicide is a transdiagnostic symptom and is associated with most mental disorders (Bertolote et al., 2004), i.e., a diagnosis of a mental disorder increases the likelihood of a suicide attempt (Gili et al., 2019). In particular, patients with a psychotic disorder or a mood disorder are more than ten times more likely to commit suicide compared to people without a mental health disorder (San Too et al., 2019). The risk for a suicide reattempt is highest in the twelve months following a suicide attempt (Dougall et al., 2014; Geddes et al., 1997; Kawanishi et al., 2014). Around 40% of people committing suicide attended a hospital emergency department in the previous twelve months (Gairin et al., 2003). Suicide, suicide attempts, and their effects on family and friends (Cerel et al., 2008) are not only psychologically burdensome on the individual, but also lead to a high financial cost for the state due to healthcare costs and other indirect costs, such as lost labor. For example, the national U.S cost in 2013 was calculated as 93.500.000.000\$ (Shepard et al., 2016). Therefore, timely interventions to prevent suicide reattempt are of great clinical and economic relevance. Given the different rates of suicide and reattempts in genders, age groups, and underlying conditions, interventions may become more effective if optimized according to patient characteristics.

#### **1.2 Description of Brief Contact Interventions**

Brief contact interventions (BCI) are low-cost interventions aiming to establish a long-term contact with patients who attempted to commit suicide (Berrouiguet et al., 2018). These interventions include phone contact, (Marasinghe et al., 2012; Mousavi et al., 2014) crisis postcards (Hassanian-Moghaddam et al., 2011), safety planning (Fleischmann et al., 2008), or a combination (Vaiva et al., 2011). The content of follow-up messages varies, but it is important to express concern for patients and to give patients a way to recontact health care

specialists (Berrouiguet et al., 2018). The low bar of entry of BICs makes it possible to reach patients, who would otherwise not receive treatment (Granboulan et al., 2001). One specific type of BCI is the brief intervention and contact-program (BIC-program) developed by the WHO (U.S. Department of Veterans Affairs, 2022). The BIC-program is more standardized than other BCIs and always includes 9 follow-up contacts over 18 months. Additionally, the BIC-program includes an individual psychoeducational program on suicide risk and a motivational interview to increase self-efficacy (U.S. Department of Veterans Affairs, 2022)

#### 1.3 Current evidence

People at risk of suicide are commonly excluded from clinical trials (Iltis et al., 2020). As a result, the amount of evidence for this population is sparse (Iltis et al., 2020). Several previous reviews and meta-analyses assessing the effects of suicide prevention interventions exist (Calear et al., 2016; Doupnik et al., 2020; Fox et al., 2020; Hofstra et al., 2020; Inagaki et al., 2015; Lapierre et al., 2011; Meerwijk et al., 2016; Robinson et al., 2018; Robinson et al., 2011; Schmelefske et al., 2022). Generally, these reviews concluded that most interventions reduce the risk of suicidal ideation and suicidal behavior compared to control interventions. However, these reviews all had multiple noteworthy methodological shortcomings, e.g. didn't assess Risk of Bias, or did not assess the overall quality of evidence (Table S1).

#### 2 Methods

#### 2.1 Objectives and Research questions

This master-thesis is part of a larger project assessing various interventions to prevent suicide reattempts. The objective of this review and meta-analysis was to assess effects of brief contact interventions in the prevention of suicide reattempts with the following research questions:

- 1. Do brief contact interventions have a higher efficacy compared to control interventions?
- 2. Does the efficacy of other brief contact interventions differ from the Brief intervention and contact-program?

- 3. Do trials at high risk of bias have a different efficacy than to trials at low risk of bias?
- 4. Do brief contact interventions have a different efficacy in men than in women?

#### 2.2 Study selection and analysis

The systematic review is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2015). The methodology used in this systematic review is described in detail in The Cochrane Handbook of Systematic Reviews of Interventions (J. P. Higgins et al., 2019).

#### 2.3 Search strategy

#### 2.3.1 Electronic search and other searches

An information specialist searched the Medical Literature Analysis and Retrieval System Online (MEDLINE), and Excerpta Medica Database (Embase) from inception to 01 December 2023. The search included the screening of references of relevant trials and similar systematic reviews. For a detailed search strategy for all electronic databases, see supplementary (Text S1). The PRISMA-flowchart for the literature search can be found in **Figure 1**.

#### 2.3.2 Selection criteria

Randomized trials published in English or German irrespective of publication year and publication type are included. Participants who were admitted to the emergency department after a recent suicide attempt (as defined by trialist) are included. Participants are included regardless of age, sex, or diagnosis. Any intervention aimed at reducing suicide-related behaviour is accepted. Any control intervention is accepted. Co-interventions are allowed provided they are administered equally to the comparison groups.

#### 2.4 Outcomes and subgroup analysis

The primary outcomes were suicide, and suicide attempts. The secondary outcomes were suicidal ideation and self-harm.

The following subgroup analyses were performed when analysing the primary outcomes (suicide, and suicide attempts):

- 1. Trials at high risk of bias compared to trials at low risk of bias
- Type of intervention (General brief contact interventions vs the Brief intervention and contact program (BIC) developed by the WHO (U.S. Department of Veterans Affairs, 2022)
- 3. Sex (male vs female)

#### 2.5 Assessment of statistical significance

Meta-Analyses were performed according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (J. Higgins et al., 2019), and the eightstep procedure (Jakobsen et al., 2014). The threshold for statistical significance was adjusted by the number of primary outcomes and therefore a *p*-value of 0.033 or less was used (Jakobsen et al., 2014). Data was analysed using the software STATA (StataCorp, 2019). Both random-effects (DerSimon and Laird) (DerSimonian & Laird, 2015) and fixed-effect model meta-analyses (Mantel-Haenszel) were used to assess intervention effects (DeMets, 1987; J. Higgins et al., 2019). The most conservative result (highest *p*-value) was primarily reported and the less conservative result was considered a sensitivity analysis (Jakobsen et al., 2014). Risk of Bias assessment (J. Higgins et al., 2019; Sterne et al., 2019) and Grading Recommendations Assessment Development Evaluation (GRADE) were used to assess the certainty of evidence (Guyatt et al., 2011; Guyatt et al., 2008; Schünemann et al., 2003). The syntax used to conduct the analysis can be found in the supplementary material (Text S2).

#### **3 Results**

A total of 15 trials randomising 8841 participants were included (Amadéo et al., 2015; Bertolote et al., 2015; Carter et al., 2013; Chen et al., 2013; Cotgrove et al., 1995; Fleischmann et al., 2008; Harrington et al., 1998; Morthorst et al., 2012; Mousavi et al., 2017; Mousavi et al., 2014; Vaiva et al., 2006; Van Heeringen et al., 1995; Vijayakumar et al., 2011; Wei et al., 2013). Most trials included adults of both genders(Amadéo et al., 2015; Bertolote et al., 2015; Carter et al., 2013; Chen et al., 2013; Fleischmann et al., 2008; Morthorst et al., 2012; Mousavi et al., 2017; Mousavi et al., 2014; Vaiva et al., 2006; Van Heeringen et al., 1995; Vijayakumar et al., 2011; Wei et al., 2013). 2 trials only included adolescents (Cotgrove et al., 1995; Harrington et al., 1998). No trials required a specific diagnosis or suicide method for inclusion. All trials were assessed at overall high risk of bias (Table S2). The maximum follow-up ranged from 6 months to 5 years with a median follow up time of 1 year. An overview of included trials with additional information can be found in the supplementary material (Table S3).

#### Figure 1:

#### PRISMA-Flowchart



#### 3.1 Primary Outcomes

#### 3.1.1 Suicide

8 trials randomising 4483 participants reported results on suicides (Amadéo et al., 2015; Carter et al., 2013; Fleischmann et al., 2008; Morthorst et al., 2012; Vaiva et al., 2006; Van Der Sande et al., 1997; Van Heeringen et al., 1995; Vijayakumar et al., 2011). Outcomes were assessed between 1 year and 5 years after randomisation. A total of 18/2229 (0.81%) experimental participants committed suicide compared with 44/2254 (1.95%) control participants. Random-effects meta-analysis showed no evidence of a beneficial effect of BCIs versus control interventions on suicide (risk ratio (RR) 0.46; 95% CI 0.22 to 0.97; p =.04; 8 trials) (**Figure 2**). Visual inspection of the forest plot and statistical tests (I<sup>2</sup> = 28.0%) indicated moderate heterogeneity that could not be resolved. Fixed-effects meta-analysis showed evidence of a beneficial effect of BCIs versus control interventions on suicide (risk ratio (RR) 0.40; 95% CI 0.23 to 0.68; p < .01; 8 trials) (Fig. S1). Visual inspection of the forest plot and statistical tests (I<sup>2</sup> = 32.50%) indicated moderate heterogeneity that could not be resolved. This outcome result was assessed as overall high risk of bias, and the certainty of the evidence was very low (**Table 1**).

#### Figure 2

Random-Effects Meta-Analysis of Brief Contact Interventions vs Control Interventions on Suicide

	Inte	rvention	С	ontrol				Risk ra	tio	Weight
Study	Suicide	No Suicide	Suicide	No Suicide	)			with 95%	5 CI	(%)
Amadeo - 2015	0	90	2	98				0.22 [ 0.01,	4.56]	5.36
Carter - 2013	6	388	5	373				1.15 [ 0.35,	3.74]	21.57
Fleischmann - 2008	2	870	18	809				0.11 [ 0.02,	0.45]	16.75
Morthorst - 2012	1	122	1	119			ļ	-0.98 [ 0.06,	15.42]	6.29
Vaiva - 2006	1	201	2	278				0.69 [ 0.06,	7.59]	8.01
Van der Sande - 1997	1	139	2	132	_			0.48 [ 0.04,	5.22]	8.04
Van Heeringen - 1995	6	190	7	188			<b>—</b>	0.85 [ 0.29,	2.49]	23.78
Vijayakumar - 2011	1	301	9	311		-	-	0.12 [ 0.02,	0.92]	10.21
Overall						-	•	0.46 [ 0.22,	0.97]	
Heterogeneity: $\tau^2 = 0.31$	$, I^2 = 28.0$	$02\%, H^2 = 1.3$	39							
Test of $\theta_i = \theta_j$ : Q(7) = 9.7	73, p = 0.	20								
Test of $\theta$ = 0: z = -2.04,	p = 0.04									
					1/64	1/8	1 8	-		

Random-effects DerSimonian-Laird model

Test of interaction comparing the effects of the BIC-program with general BCIs showed evidence of a difference (p < .01) in favour of the BIC-program (Fig S2). An additional analysis showed evidence of a beneficial effect of BIC-program versus control interventions (p < .01) (Fig. S3, Fig. S4). Remaining predefined subgroup analyses could not be performed due to a lack of relevant data.

#### 3.1.2 Suicide attempt

13 trials randomising 7099 participants reported results on suicide attempts (Amadéo et al., 2015; Bertolote et al., 2015; Carter et al., 2013; Cotgrove et al., 1995; Hassanian-Moghaddam et al., 2017; Morthorst et al., 2012; Mousavi et al., 2017; Mousavi et al., 2014; Vaiva et al., 2006; Van Der Sande et al., 1997; Van Heeringen et al., 1995; Vijayakumar et al., 2011; Wei et al., 2013). Outcomes were assessed between 6 months and 5 years after randomisation. A total of 363/3533 (10.27%) experimental participants committed suicide compared with 435/3566 (12.20%) control participants. Random-effects meta-analysis showed no evidence of a beneficial effect of BCIs versus control interventions on suicide (risk ratio (RR) 0.87; 95% CI 0.72 to 1.05; p = .14; 13 trials) (Figure 3). Visual inspection of the forest plot and statistical tests ( $I^2 = 38.51\%$ ) indicated moderate heterogeneity that could not be resolved. Fixed-effects meta-analysis showed evidence of a beneficial effect of BCIs versus control interventions on suicide (risk ratio (RR) 0.86; 95% CI 0.75 to 0.97; p =.02; 13 trials) (Fig S5). Visual inspection of the forest plot and statistical tests ( $I^2 = 38.75\%$ ) indicated moderate heterogeneity that could not be resolved. This outcome result was assessed as overall high risk of bias, and the certainty of the evidence was very low (Table 1).

#### Figure 3

Random-Effects Meta-Analysis of Brief Contact Interventions vs Control Interventions on Suicide Attempts

	Inte	rvention	C	Control		Risk ratio	Weight
Study	Suicide attempt	No Suicide attempt	Suicide attempt	No Suicide attemp	t	with 95% CI	(%)
Amadeo - 2015	24	66	21	79		1.27 [ 0.76, 2.12]	8.92
Carter - 2013	94	300	107	271		0.84 [ 0.66, 1.07]	17.76
Cotgrove -1995	3	44	7	51		0.53 [ 0.14, 1.93]	2.01
Fleischmann - 2008	66	797	60	740		1.02 [ 0.73, 1.43]	13.97
Hassanian-Moghaddam - 2015	62	935	91	913		0.69 [ 0.50, 0.94]	14.90
Morthorst - 2012	20	103	13	107		-1.50 [ 0.78, 2.88]	6.40
Mousavi - 2013	1	68	4	66		0.25 [ 0.03, 2.21]	0.76
Mousavi - 2017	2	28	6	24		0.33 [ 0.07, 1.52]	1.50
Vaiva - 2006	44	158	59	221	+	1.03 [ 0.73, 1.46]	13.62
Van der Sande - 1997	23	117	18	116		1.22 [ 0.69, 2.16]	7.75
Van Heeringen - 1995	15	181	27	168		0.55 [ 0.30, 1.01]	7.22
Vijayakumar - 2011	8	294	17	303		0.50 [ 0.22, 1.14]	4.42
Wei - 2012	1	79	5	72		0.19 [ 0.02, 1.61]	0.79
Overall					•	0.87 [ 0.72, 1.05]	
Heterogeneity: $\tau^2 = 0.04$ , $I^2 = 38$ .	51%, H <sup>2</sup> = 1.63						
Test of $\theta_i = \theta_j$ : Q(12) = 19.51, p =	0.08						
Test of θ = 0: z = -1.46, p = 0.14							
					1/32 1/8 1/2 2	-	
Random-effects DerSimonian-Lai	rd model						

Test of interaction comparing the effects of sex showed no evidence of a difference (p = .98) (Fig S6). Test of interaction comparing the effects of the BIC-program with general BCIs showed no evidence of a difference (p = .51) (Fig. S7). The remaining predefined subgroup analyses could not be performed due to a lack of relevant data.

#### Table 1

#### Grade Assessment: Brief contact interventions vs control interventions

Certainty assessment						№ of p	atients	Ef	fect			
№ of studie s	Study design	Risk of bias	Inconsisten cy	Indirectne ss	Imprecisi on	Other consideratio ns	brief contact interventio ns	control interventio ns	Relativ e (95% CI)	Absolut e (95% Cl)	Certainty	Importan ce

Suicide (follow-up: range 1 year to 5 years)

8	randomis ed trials	very seriou sª	not serious	not serious	very serious <sup>1,b</sup>	strong association	36/4458 (0.8%)	88/4508 (2.0%)	RR 0.46 (0.22 to 0.97)	11 fewer per 1.000 (from 15 fewer to 1 fewer)	⊕⊖⊖ Very low	

Suicide attempt (follow-up: range 4 months to 5 years)

13	randomis ed trials	very seriou sª	not serious	not serious	very serious <sup>1,c</sup>	none	363/3533 (10.3%)	435/3566 (12.2%)	<b>RR</b> <b>0.87</b> (0.72 to 1.05)	16 fewer per 1.000 (from 34 fewer to 6 more)	⊕⊖⊖ O Very low	
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CI: confidence interval; RR: risk ratio; a. Downgraded 2 for High Risk of Bias in Included Studies; b. Not statistical significant but the lower boundry of the CI suggests a reduction of suicides by almost 80%; c. Not statistical significant but the lower boundry of the CI suggests a reduction of suicides by almost 30%

#### 3.2 Secondary Outcomes

#### 3.2.1 Self-harm

The predefined meta-analysis could not be performed due to a lack of relevant data.

#### 3.2.2 Suicidal ideation

The predefined meta-analysis could not be performed due to a lack of relevant data.

#### **4 Discussion**

#### 4.1 Summary

This systematic review and meta-analysis assessed the efficacy of BCI compared to control interventions for participants with a recent suicide attempt. A total of 15 trials randomising 8841 participants were included. All outcome results were at overall high risk of bias and the certainty of evidence was very low, mostly due to the lack of blinding, missing data, and the lack of preregistered protocols.

# 4.1.1 Do brief contact interventions have a higher efficacy compared to control interventions?

Meta-Analysis showed no evidence of a significant difference between BCIs and control interventions for suicides (p = .04) and suicide attempts (p = .14). This is in line with the current evidence (Mann et al., 2005; Riblet et al., 2017; Zalsman et al., 2016). Milner et al. (2015) found a significant reduction in suicide attempts, though. This difference may be due to the fact that they included non-randomized trials that could distort the true effect (Kunz & Oxman, 1998). It was not possible to compare participants between this study and that of Milner et al. (2015), as the inclusion criteria were not properly described.

# 4.1.2 Does the efficacy of other brief contact interventions differ from the Brief intervention and contact-program?

Subgroup analysis showed that the BIC-program is more effective than BCI (p < .01) in preventing suicides. This is in line with the findings of Riblet (2017). This difference could be explained by the longer intervention time of 1,5 years in BIC compared to the 1-year median intervention time in other BCIs. Riblet (2019) found evidence that a long contact time leads to a higher sense of connectedness and support which are 2 important factors to prevent suicide attempts (Gutierrez et al., 2016; Kleiman & Liu, 2013). The authors also propose that psychoeducation and the motivational interview led to a higher motivation to engage in outpatient treatment to reduce underlying mental health problems which in turn reduces suicide attempts (Hawton et al., 2013).

The BIC-program was so far mostly used in low-income countries (Fleischmann et al., 2008), making its transferability unclear. While first pilot studies were conducted (Riblet et al., 2019), larger, randomised controlled trials are needed ensure effectiveness. Further research should examine whether the initially reported effect remains when used in high-

income countries. Moreover, potential moderators and mediators of the program's efficacy, such as mental illness, suicide method, or demographic characteristics have not yet been inspected and warrant further research.

# 4.1.3 Do trials at high risk of bias have a different efficacy than to trials at low risk of bias?

All trials were rated at high risk of bias (mostly due to the lack of blinding), and it was not possible to conduct this subgroup analysis. Blinding is a known problem in psychological trials (Juul et al., 2020). A lack of blinding has a large impact on estimated treatment effects (Savović et al., 2018) and often leads to inflated effect sizes (Schulz et al., 1995). This is underlined by the fact that the only trial that attempted to blind outcome assessors (Morthorst et al., 2012) had the highest risk ratio regarding suicide attempts (risk ratio (RR) 1.50; 95% CI 0.78 to 2.88).

#### 4.1.4 Do brief contact interventions have a different efficacy in men than in women?

Subgroup analysis did not show a different effect between men and women (p = .98) on suicide attempts. Only 3 trials reported a gender-specific outcome (Morthorst et al., 2012; Mousavi et al., 2017; Mousavi et al., 2014) including a total of 396 participants, so the power may have been too low to detect a significant effect. Previous evidence is sparse and no other systematic review on suicide reattempts tried assessing gender differences. One illustrative review assessing the gender differences in primary prevention showed that girls profit from interventions more than boys (Hamilton & Klimes-Dougan, 2015) but there is no evidence to support that these findings also apply to a secondary prevention

#### 4.2 Strengths and Limitations

This review has several strengths. The review was conducted using a rigorous methodological approach based on the Cochrane Handbook for Systematic Reviews of Interventions, PRISMA, the eight-step procedure by Jakobsen et al, the GRADE approach, and heterogeneity were considered. Subgroup analyses were conducted, and statistical significance was adjusted due to multiple testing. The primary outcomes chosen are binary and of high clinical importance.

The review also has several limitations. First, suicide is a very rare outcome (0.81%/1.95%) in this review) which makes it difficult to detect a significant effect. Second, due to time

constraints, it was not possible to search for and include unpublished trials. In particular, trials with a non-significant result tend to remain unpublished (Song et al., 2010), which might lead to an overestimation of the intervention effect in this systematic review. Third, while the statistical significance was adjusted according to the number of primary outcomes, it was not adjusted for the secondary analyses and subgroups analyses. Fourth, the control interventions were often poorly described and might be very heterogeneous, possibly explaining the heterogeneity in the meta-analyses. Fifth, only 1 person conducted the screening of trials and data extraction. This increases the chance of human error, and it was not possible to test the inter-rater reliability. Sixth, Trial Sequential Analysis was not conducted and it is therefore not possible to assess whether or not this meta-analysis is underpowered (Brok et al., 2008; Wetterslev et al., 2008).

#### **5** Conclusion and clinical implication

The more structured brief intervention and contact program by the World Health Organisation appears to be more effective than general brief contact interventions. Due to its low cost of implementation, it is advisable to offer the brief intervention and contact program for patients with a recent suicide attempt.

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### Eigenständigkeitserklärung



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Hiermit erkläre ich, dass ich die vorliegende Arbeit eigenständig ohne fremde Hilfe und nur unter Verwendung der angegebenen Hilfsmittel angefertigt habe. Alle sinngemäß und wörtlich übernommenen Textstellen aus der Literatur bzw. dem Internet habe ich als solche kenntlich gemacht.

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