National Institute for Health and Care Excellence

Final

Self-harm: assessment, management and preventing recurrence

[K] Evidence reviews for pharmacological interventions

NICE guideline number NG225

Evidence reviews underpinning recommendation 1.11.10 in the NICE guideline

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Final

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What pharmacological interventions are effective for people who have self-harmed?

Introduction

Evidence assessing the effectiveness of pharmacological agents and/ or natural products in the treatment of self-harm is lacking, especially when compared with the evidence for psychosocial interventions. Whilst there has been an increase in the use of psychosocial interventions for self-harm, drug treatments are frequently used in clinical practice. The aim of this review is to assess the effects of pharmacological agents or natural products for self-harm compared to comparison types of treatment (for example, placebo or alternative pharmacological treatment) for people who have self-harmed.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	**Inclusion:** Children, adolescents and adults who had engaged in any type of non-fatal intentional self-poisoning or self-injury in the six months prior to trial entry resulting in presentation to clinical services. **Exclusion:** • Children, adolescents and adults who had presented to clinical services as a result of repetitive stereotypical self-injurious behaviours, for example, head-banging in people with a significant learning disability. • Trials where only some people had engaged in self-harm or where self-harm was an outcome variable, but not an inclusion criteria for entry into the trial.
Intervention	Any pharmacological interventions, for example: • Tricyclic antidepressants (TADs; for example, amitriptyline) • Newer generation antidepressants (NGAs), such as selective serotonin reuptake inhibitors (SSRIs; for example, fluoxetine), serotonin and noradrenaline reuptake inhibitors (SNRIs; for example, venlafaxine), norepinephrine reuptake inhibitors (NRIs; for example, reboxetine), tetracyclic antidepressants (for example, maprotiline), noradrenergic specific serotonergic antidepressants, (NaSSAs; for example, mirtazapine), serotonin antagonist or reuptake inhibitors (SARIs; for example, trazodone), or reversible inhibitors of monoamine oxidase type A (RIMAs; for example, moclobemide)

	• Any other antidepressants, such as irreversible monoamine oxidase inhibitors (MAOIs; for example, bupropion) • Antipsychotics (for example, quetiapine) • Anxiolytics, including both benzodiazepines and non-benzodiazepines anxiolytics • Mood stabilisers, including antiepileptics (for example, sodium valproate) and lithium • Other pharmacological agents (for example, benzodiazepines, ketamine) • Natural products (for example, omega-3 essential fatty acid supplementation) **Exclusion:** Pharmacological treatment of any mental health problems or substance use disorders that may co-exist/be associated with self-harm, that is, direct pharmacological treatment of any such problem or condition itself is excluded
Comparison	• Placebo • Another pharmacological intervention • Reduced dose of pharmacological intervention
Outcome	**Critical** • Occurrence/repetition of self-harm (measured by self/collateral report, clinical records or research monitoring) • Proportion of participants repeating self-harm • Frequency of self-harm (measured by self/collateral report, clinical records or research monitoring) • Time to self-harm Maximum follow-up period of 2 years. This will be grouped into: at conclusion of the treatment period, 0-6 months after the conclusion of treatment, 6-12 months after the conclusion of treatment, 12-24 months after the conclusion of treatment. **Important** • Treatment adherence (started and completed treatment) • Depression (measured continuously by psychometric assessments or dichotomously as proportion reaching defined diagnostic criteria) • Hopelessness (measured by psychometric assessments) • General functioning (measured by psychometric assessments) • Social functioning (measured by psychometric assessments) • Suicidal ideation (measured continuously by psychometric assessments or dichotomously as proportion reaching defined cut-off for ideation)

	• Suicide (measured by register recorded deaths and collateral report) Maximum follow-up period of 2 years. This will be grouped into: during treatment, at conclusion of the treatment period, 0-6 months after the conclusion of treatment, 6-12 months after the conclusion of treatment, 12-24 months after the conclusion of treatment.

For further details see the review protocol in appendix A.

Methods and process

During the development of this guideline, two registered Cochrane protocols were identified which matched the committee's intended PICOs. The Cochrane protocols differed from the committee's intended population in that the Cochrane protocols excluded studies that included people who had self-harmed who had a neurodevelopmental disorder or learning difficulty, however no studies were identified that were excluded from the reviews on these grounds alone.

The Cochrane review team completed two reviews investigating the effectiveness of pharmacological interventions in adults (Witt 2021a) and psychosocial and pharmacological interventions in children and young people (CYP) (Witt 2021b) during guideline development and presented their results to the guideline committee, who used them to make recommendations. Cochrane's methods are closely aligned to standard NICE methods; minor deviations (the use of GRADE only on main outcomes with no overall quality rating for those with zero events in either arm, summary of findings tables instead of full GRADE tables, defining primary and secondary outcomes as opposed to critical and important and including countries from a broader range of income categories than the majority of the other reviews in the guideline) relevant to the topic area were highlighted to the committee and taken into account in discussions of the evidence.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

Two Cochrane reviews (Witt 2021a, Witt 2021b) including 7 randomised controlled trials (Battaglia 1999, Hallahan 2007, Hirsch 1982, Lauterbach 2008, Montgomery 1979, Montgomery 1983, Verkes 1998) were considered in this report. All included studies were from the review investigating pharmacological interventions for adults, as no pharmacological studies were identified which were applicable to the review investigating interventions for children who had self-harmed. These reviews were used for recommendation making by the committee, as they were considered sufficiently relevant, high quality and up to date.

The Cochrane reviews are summarised in Table 2, however full details of the Cochrane reviews including methods are available in the review of Pharmacological interventions for self-harm in adults and the review of Interventions for self-harm in children and adolescents.

See the Cochrane reviews for the literature search strategies for the adults review and the CYP review, study selection flow charts for the adults review and the CYP review, forest plots in the adults review and the CYP review, and summary of findings tables for the adults review and the CYP review.

Excluded studies

See the lists of excluded studies in the Cochrane adults review and the CYP review with reasons for their exclusions.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Comparison	Outcomes
Witt 2021a Systematic review	Number of studies: 7 Number of participants: 574	**Newer generation antidepressants (NGAs) versus placebo** 3 RCTs, N=263 adults who have self-harmed (Hirsch 1982, Montgomery 1983, Verkes 1998) **Antipsychotics versus placebo** 1 RCT, N=37 adults who have self-harmed (Montgomery 1979) **Antipsychotics versus another comparator drug or dose** 1 RCT, N=58 adults who have self-harmed (Battaglia 1999) **Mood stabilisers, including antiepileptics and lithium versus placebo** 1 RCT, N=167 adults who have self-harmed (Lauterbach 2008) **Natural products versus placebo** 1 RCT, N=49 adults who have self-harmed (Hallahan 2007) No eligible trials were identified for the following comparisons: • Tricyclic antidepressants versus placebo • Tricyclic antidepressants versus another comparator drug or dose • Newer generation antidepressants versus another comparator drug or dose • Any other antidepressants versus placebo • Any other antidepressants versus another comparator drug or dose • Anxiolytics, including benzodiazepines and non-benzodiazepine anxiolytics, versus placebo • Anxiolytics, including benzodiazepines and non-	Primary outcome: • Repetition of SH Secondary outcomes: • Treatment acceptability • Treatment adherence • Depression • Hopelessness • General functioning • Social functioning • Suicidal ideation • Suicide

Study	Population	Comparison	Outcomes
		benzodiazepine anxiolytics, versus another comparator drug or dose • Mood stabilisers, including antiepileptics and lithium, versus another comparator drug or dose • Other pharmacological agents versus placebo • Other pharmacological agents versus another comparator drug or dose • Natural products versus another comparator drug or dose	
Witt 2021b Systematic review	Number of studies: 0* Number of participants (CYP): 0 *Review included studies investigating psychosocial interventions but no pharmacological studies were included	No eligible trials were identified for the following comparisons: • Tricyclic antidepressants versus placebo or other comparator drug or dose • Newer generation antidepressants versus placebo or other comparator drug or dose • Any other antidepressants versus placebo or other comparator drug or dose • Antipsychotics versus placebo or other comparator drug or dose • Anxiolytics, including benzodiazepines and non-benzodiazepine anxiolytics, versus placebo or other comparator drug or dose • Mood stabilisers, including antiepileptics and lithium, versus placebo or other comparator drug or dose • Other pharmacological agents versus placebo or other comparator drug or dose • Natural products versus placebo or other comparator drug or dose	Primary outcome: • Repetition of SH over a maximum follow-up period of 2 years Secondary outcomes: • Treatment adherence • Depression • Hopelessness • General functioning • Social functioning • Suicidal ideation • Suicide • Other

CYP: children and young people; N: number; RCT: randomised controlled trial; SH: self-harm

See the Cochrane adults review and CYP review for characteristics of studies tables.

Summary of the evidence

See the Cochrane adults review and the CYP review for summary of findings tables.

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline but no economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

Economic studies not included in the guideline economic literature review are listed, and reasons for their exclusion are provided in appendix J.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

The Cochrane protocols' primary outcome was occurrence of repeated self-harm within a maximum follow-up period of 2 years, which the committee agreed is critical as it is a direct measure of any differential effectiveness associated with the pharmacological intervention. All other outcomes listed in the Cochrane protocol (treatment acceptability [for adults only]; treatment adherence; depression; hopelessness; general functioning; social functioning; suicidal ideation; suicide) were agreed to be important outcomes by the committee. The committee agreed that treatment acceptability was an important outcome for adults due to the importance of delivering services which are centred on the patients' experiences and individual needs, whereas treatment engagement would indicate the patient's satisfaction with the intervention and ultimately determine its success. Depression, hopelessness, and suicidal ideation were agreed to be important outcomes as they are measures of well-being which may capture long-term health-related outcomes associated with the effectiveness of interventions. The committee agreed that general functioning and social functioning were also important as measures of how successful the intervention is at reducing the impact of self-harm on the person's day-to-day life and ability to build and maintain relationships. Suicide was also agreed by the committee to be a direct measure of any differential effectiveness associated with the pharmacological intervention.

The quality of the evidence

There was no evidence available for many of the comparisons for adults that the committee were interested in and no evidence available at all for the effects of pharmacological interventions for children (as outlined in Table 2). For the comparisons where there was evidence that the Cochrane team applied GRADE to, it was low to very low quality and downgraded typically due to risk of bias as per Cochrane RoB 2.0 (primarily due to concerns regarding bias in the measurement of the outcome and in the selection of the reported result), imprecision (small sample size and the 95% confidence intervals included the null value) and indirectness (older agents investigated, no information on how self-harm was ascertained/ self-harm prevalence estimates derived from self-report).

The committee agreed not to make a research recommendation despite the lack of evidence because they agreed research into the efficacy of pharmacological interventions for comorbidities commonly associated with self-harm would be more useful, which was beyond the scope of the guideline.

Benefits and harms

There was no new evidence evaluating the effect of pharmacological interventions for children and adolescents or for adults who self-harm. For adults, the evidence was of low or very-low quality and showed an uncertain effect of newer generation antidepressants or antipsychotics on repetition of self-harm, and no evidence of effect of mood stabilisers or for

natural products on repetition of self-harm. There was no available evidence for children and young people who self-harm.

Due to the limited evidence, the committee agreed that it was not appropriate to offer drug treatment specifically for the purpose of reducing self-harm. The recommendation not to offer drug treatment was therefore based on the committee's knowledge that drug treatment may be offered for other coexisting conditions such as depression as well as the committee's lack of certainty in the evidence regarding the effect of pharmacological interventions on self-harm in isolation of any coexisting conditions.

Cost effectiveness and resource use

The committee noted that no relevant published economic evaluations had been identified on the cost-effectiveness of pharmacological interventions for people who have self-harmed. In addition, no additional economic analysis had been undertaken on this topic, as the committee agreed that clinicians would not commonly use medication to treat self-harm itself, but comorbidities such as depression or psychosis. Given the very high variation in current clinical practice across the NHS, and the paucity of both clinical and economic evidence, the committee decided to make a recommendation to prevent the use of medication as a specific intervention to reduce self-harm. This is expected to reduce variation in clinical practice and result in cost-savings to the health service.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.11.10.

References – included studies

Effectiveness

Witt 2021a

Witt KG, Hetrick SE, Rajaram G, Hazell P, Taylor Salisbury TL, Townsend E, Hawton K., Pharmacological interventions for self-harm in adults. Cochrane Database of Systematic Reviews 2021, Issue 1. Art. No.: CD013669. DOI: 10.1002/14651858.CD013669.pub2.

Witt 2021b

Witt KG, Hetrick SE, Rajaram G, Hazell P, Taylor Salisbury TL, Townsend E, Hawton K. Interventions for self-harm in children and adolescents. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013667. DOI: 10.1002/14651858.CD013667.pub2.

Economic

No studies were identified that met the inclusion criteria.

Appendices

Appendix A Review protocols

Review protocol for review question: What pharmacological interventions are effective for people who have self-harmed?

See the Cochrane review protocols for Pharmacological interventions for self-harm in adults and Interventions for self-harm in children and adolescents.

Appendix B Literature search strategies

Literature search strategies for review question: What pharmacological interventions are effective for people who have self-harmed?

Clinical

See Appendix 1 and Appendix 2 of the Cochrane review of Pharmacological interventions for self-harm in adults and the Appendix 1 and Appendix 2 of the Cochrane review of Interventions for self-harm in children and adolescents.

Economic

A global, population based search was undertaken to find for economic evidence covering all parts of the guideline.

Database(s): MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily – OVID interface
Date of last search: 12th August 2021

#	Searches
1	poisoning/ or exp self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ or suicide, completed/
2	(automutilat* or auto mutilat* or cutt* or (self adj2 cut*) or selfdestruct* or self destruct* or selfharm* or self harm* or selfimmolat* or self immolat* or selfinflict* or self inflict* or selfinjur* or self injur* or selfmutilat* or self mutilat* or selfpoison* or self poison* or selfwound* or self wound* or suicid*).ti,ab.
3	or/1-2
4	Economics/
5	Value of life/
6	exp "Costs and Cost Analysis"/
7	exp Economics, Hospital/
8	exp Economics, Medical/
9	Economics, Nursing/
10	Economics, Pharmaceutical/
11	exp "Fees and Charges"/
12	exp Budgets/
13	budget*.ti,ab.
14	cost*.ti.
15	(economic* or pharmaco?economic*).ti.
16	(price* or pricing*).ti,ab.
17	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
18	(financ* or fee or fees).ti,ab.
19	(value adj2 (money or monetary)).ti,ab.
20	Quality-Adjusted Life Years/
21	Or/4-20
22	3 and 21
23	limit 22 to yr="2000 -current"

Database(s): Embase and Emcare – OVID interface
Date of last search: 12th August 2021

#	searches
1	automutilation/ or exp suicidal behavior/
2	(auto mutilat* or automutilat* or self cut* or selfcut* or self destruct* or selfdestruct* or self harm* or selfharm* or self immolat* or selfimmolat* or self inflict* or selfinflict* or self injur* or selfinjur* or self mutilat* or selfmutilat* or self poison* or selfpoison* or suicid*).ti,ab.
3	or/1-2
4	health economics/
5	exp economic evaluation/
6	exp health care cost/
7	exp fee/
8	budget/
9	funding/
10	budget*.ti,ab.
11	cost*.ti.
12	(economic* or pharmaco?economic*).ti.
13	(price* or pricing*).ti,ab.
14	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15	(financ* or fee or fees).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	Quality-Adjusted Life Year/
18	Or/4-17
19	3 and 18
20	limit 19 to yr="2000 -current"

Database(s): Cochrane Library - Wiley interface
Cochrane Central Register of Controlled Trials, Issue 8 of 12, August 2021
Date of last search: 12th August 2021

#	Searches
1	MeSH descriptor: [poisoning] this term only
2	MeSH descriptor: [self-injurious behavior] explode all trees

#	Searches
3	MeSH descriptor: [self mutilation] this term only
4	MeSH descriptor: [suicide] this term only
5	MeSH descriptor: [suicidal ideation] this term only
6	MeSH descriptor: [suicide, attempted] this term only
7	MeSH descriptor: [suicide, completed] this term only
8	(automutilat* or "auto mutilat*" or cutt* or (self near/2 cut*) or selfdestruct* or "self destruct*" or selfharm* or "self harm*" or selfimmolat* or "self immolat*" or selfinflict* or "self inflict*" or selfinjur* or "self injur*" or selfmutilat* or "self mutilat*" or selfpoison* or "self poison*" or selfwound* or "self wound*" or suicid*):ti,ab.
9	{or #1-#8}
10	MeSH descriptor: [Economics] this term only
11	MeSH descriptor: [Value of life] this term only
12	MeSH descriptor: [Costs and Cost Analysis] explode all trees
13	MeSH descriptor: [Economics, Hospital] explode all trees
14	MeSH descriptor: [Economics, Medical] explode all trees
15	MeSH descriptor: [Economics, Nursing] this term only
16	MeSH descriptor: [Economics, Pharmaceutical] this term only
17	MeSH descriptor: [Fees and Charges"]
18	MeSH descriptor: [Budgets] this term only
19	budget*:ti,ab.
20	cost*.ti.
21	(economic* or pharmaco?economic*):ti.
22	(price* or pricing*):ti,ab.
23	(cost* near/2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)):ab.
24	(financ* or fee or fees):ti,ab.
25	(value near/2 (money or monetary)):ti,ab.
26	MeSH descriptor: [Quality-Adjusted Life Years] this term only
27	{OR #10-#26}
28	(#9 and #27) with Cochrane Library publication date Between Jan 2000 and Aug 2021

Database(s): NHS EED and HTA – CRD interface
Date of last search: 12th August 2021

#	Searches
1	MeSH descriptor: poisoning IN NHSEED, HTA
2	MeSH descriptor: self-injurious behavior EXPLODE ALL TREES IN NHSEED, HTA
3	MeSH descriptor: self mutilation IN NHSEED, HTA
4	MeSH descriptor: suicide IN NHSEED, HTA
5	MeSH descriptor: suicidal ideation IN NHSEED, HTA
6	MeSH descriptor: suicide, attempted IN NHSEED, HTA
7	MeSH descriptor: suicide, completed IN NHSEED, HTA
8	(automutilat* or "auto mutilat*" or cutt* or (self near2 cut*) or selfdestruct* or "self destruct*" or selfharm* or "self harm*" or selfimmolat* or "self immolat*" or selfinflict* or

#	Searches
	"self inflict*" or selfinjur* or "self injur*" or selfmutilat* or "self mutilat*" or selfpoison* or "self poison*" or selfwound* or "self wound*" or suicid*) IN NHSEED, HTA
9	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) from 2000 to 2021

Appendix C Results of the search

Results of the search for review question: What pharmacological interventions are effective for people who have self-harmed?

See Results of the search – figure 1 from the Cochrane review of Pharmacological interventions for self-harm in adults and Results of the search – figure 1 from the Cochrane review of Interventions for self-harm in children and adolescents.

Appendix D Characteristics of studies tables

Characteristics of studies tables for review question: What pharmacological interventions are effective for people who have self-harmed?

See the Characteristics of included studies tables from the Cochrane review of Pharmacological interventions for self-harm in adults and the Characteristics of included studies tables from the Cochrane review of Interventions for self-harm in children and adolescents.

Appendix E Data and analyses

Data and analyses for review question: What pharmacological interventions are effective for people who have self-harmed?

See the Data and analyses tables from the Cochrane review of Pharmacological interventions for self-harm in adults and the Data and analyses tables from the Cochrane review of Interventions for self-harm in children and adolescents.

Appendix F Summary of findings tables

Summary of findings tables for review question: What pharmacological interventions are effective for people who have self-harmed?

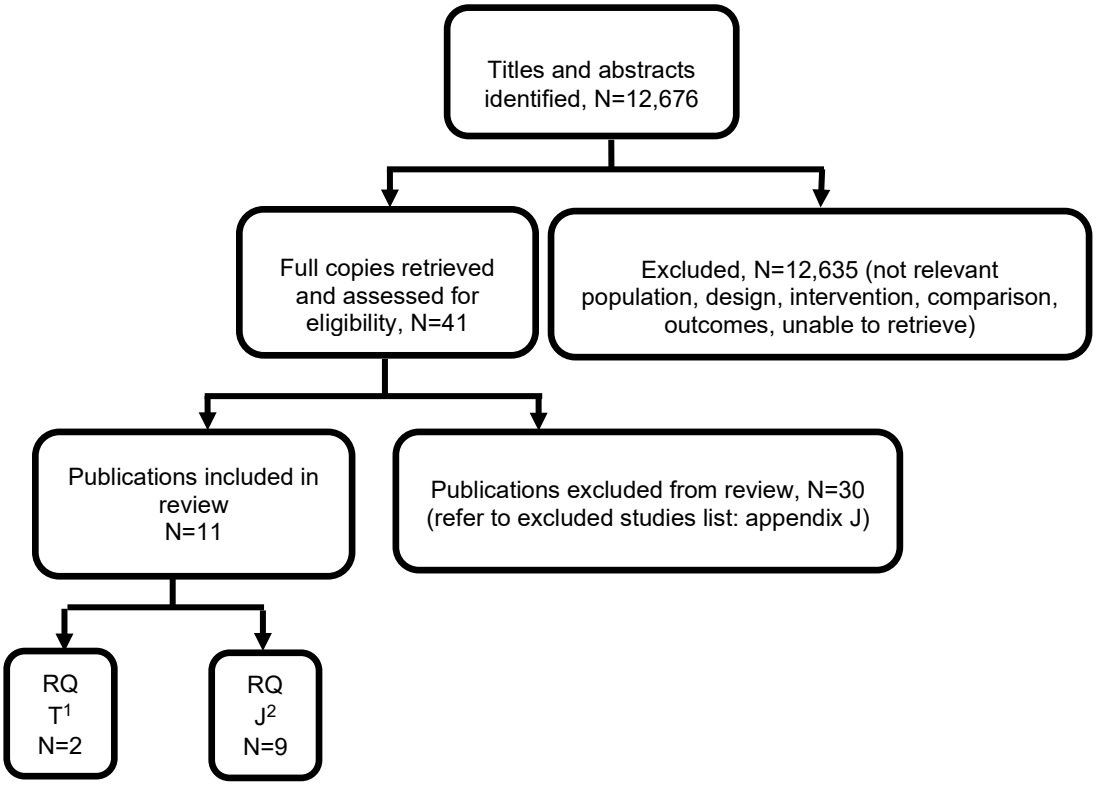
See the Summary of findings tables from the Cochrane review of Pharmacological interventions for self-harm in adults and the Summary of findings tables from the Cochrane review of Interventions for self-harm in children and adolescents.

Appendix G Economic evidence study selection

Study selection for review question: What pharmacological interventions are effective for people who have self-harmed?

A global health economics search was undertaken for all areas covered in the guideline. Figure 1 shows the flow diagram of the selection process for economic evaluations of interventions and strategies associated with the care of people who have self-harmed.

Figure 1: Flow diagram of economic article selection for global health economic search



Abbreviations: RQ: Research question
Notes:
1 What are the most effective models of care for people who have self-harmed?
2 What psychological and psychosocial interventions (including safety plans and electronic health-based interventions) are effective for people who have self-harmed?

Appendix H Economic evidence tables

Economic evidence tables for review question: What pharmacological interventions are effective for people who have self-harmed?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What pharmacological interventions are effective for people who have self-harmed?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What pharmacological interventions are effective for people who have self-harmed?

Excluded effectiveness studies

See the Characteristics of excluded studies table from the Cochrane review of Pharmacological interventions for self-harm in adults and the Characteristics of excluded studies table from the Cochrane review of Interventions for self-harm in children and adolescents.

Excluded economic studies

Table 3: Excluded studies from the guideline economic review

Study	Reason for Exclusion
Adrian, M., Lyon, A. R., Nicodimos, S., Pullmann, M. D., McCauley, E., Enhanced "Train and Hope" for Scalable, Cost-Effective Professional Development in Youth Suicide Prevention, Crisis, 39, 235-246, 2018	Not relevant to any of the review questions in the guideline - this study examined the impact of an educational training ongoing intervention, and the effect of the post-training reminder system, on mental health practitioners' knowledge, attitudes, and behaviour surrounding suicide assessment and intervention. As well, this study was not a full health economic evaluation
Borschmann R, Barrett B, Hellier JM, et al. Joint crisis plans for people with borderline personality disorder: feasibility and outcomes in a randomised controlled trial. Br J Psychiatry. 2013;202(5):357-364.	Not relevant to any of the review questions in the guideline - this study examined the feasibility of recruiting and retaining adults with borderline personality disorder to a pilot randomised controlled trial investigating the potential efficacy and cost-effectiveness of using a joint crisis plan
Bustamante Madsen, L., Eddleston, M., Schultz Hansen, K., Konradsen, F., Quality Assessment of Economic Evaluations of Suicide and Self-Harm Interventions, Crisis, 39, 82-95, 2018	Study design - this review of health economics studies has been excluded for this guideline, but its references have been hand-searched for any relevant health economic study
Byford, S., Barrett, B., Aglan, A., Harrington, V., Burroughs, H., Kerfoot, M., Harrington, R. C., Lifetime and current costs of supporting young adults who deliberately poisoned themselves in childhood and adolescence, Journal of Mental Health, 18, 297-306, 2009	Study design – no comparative cost analysis
Byford, S., Leese, M., Knapp, M., Seivewright, H., Cameron, S., Jones, V., Davidson, K., Tyrer, P., Comparison of alternative methods of collection of service use data for the economic evaluation health care interventions, Health Economics, 16, 531-536, 2007	Study design – no comparative cost analysis
Byford, Sarah, Barber, Julie A., Harrington, Richard, Barber, Baruch Beautrais Blough Brent Brodie Byford Carlson Chernoff Collett Fergusson Garland Goldberg Harman Harrington Hawton Huber Kazdin Kazdin Kerfoot Kerfoot Kerfoot Knapp Lindsey McCullagh Miller Netten Reynolds Sadowski Shaffer Simms Wu, Factors that influence the cost of deliberate self-poisoning in children and adolescents, Journal of Mental Health Policy and Economics, 4, 113-121, 2001	Study design – no comparative cost analysis

Study	Reason for Exclusion
Denchev, P., Pearson, J. L., Allen, M. H., Claassen, C. A., Currier, G. W., Zatzick, D. F., Schoenbaum, M., Modeling the cost-effectiveness of interventions to reduce suicide risk among hospital emergency department patients, Psychiatric Services, 69, 23-31, 2018	Not relevant to any of the review questions in the guideline - this study estimated the cost-effectiveness of outpatient interventions (Postcards, Telephone outreach, Cognitive Behaviour Therapy) to reduce suicide risk among patients presenting to general hospital emergency departments
Dunlap, L. J., Orme, S., Zarkin, G. A., Arias, S. A., Miller, I. W., Camargo, C. A., Sullivan, A. F., Allen, M. H., Goldstein, A. B., Manton, A. P., Clark, R., Boudreaux, E. D., Screening and Intervention for Suicide Prevention: A Cost-Effectiveness Analysis of the ED-SAFE Interventions, Psychiatric services (Washington, D.C.), appips201800445, 2019	Not relevant to any of the review questions in the guideline - this study estimated the cost-effectiveness of suicide screening followed by an intervention to identify suicidal individuals and prevent recurring self-harm
Fernando, S. M., Reardon, P. M., Ball, I. M., van Katwyk, S., Thavorn, K., Tanuseputro, P., Rosenberg, E., Kyeremanteng, K., Outcomes and Costs of Patients Admitted to the Intensive Care Unit Due to Accidental or Intentional Poisoning, Journal of Intensive Care Medicine, 35, 386-393, 2020	Study design – no comparative cost analysis
Flood, C., Bowers, L., Parkin, D., Estimating the costs of conflict and containment on adult acute inpatient psychiatric wards, Nursing economic$, 26, 325-330, 324, 2008	Study design – no comparative cost analysis
Fortune, Z., Barrett, B., Armstrong, D., Coid, J., Crawford, M., Mudd, D., Rose, D., Slade, M., Spence, R., Tyrer, P., Moran, P., Clinical and economic outcomes from the UK pilot psychiatric services for personality-disordered offenders, International Review of Psychiatry, 23, 61-9, 2011	Not relevant to any of the review questions in the guideline
George, S., Javed, M., Hemington-Gorse, S., Wilson-Jones, N., Epidemiology and financial implications of self-inflicted burns, Burns, 42, 196-201, 2016	Study design – no comparative cost analysis
Gunnell, D., Shepherd, M., Evans, M., Are recent increases in deliberate self-harm associated with changes in socio-economic conditions? An ecological analysis of patterns of deliberate self-harm in Bristol 1972-3 and 1995-6, Psychological medicine, 30, 1197-1203, 2000	Study design - cost-of-illness study
Kapur, N., House, A., Dodgson, K., Chris, M., Marshall, S., Tomenson, B., Creed, F., Management and costs of deliberate self-poisoning in the general hospital: A multi-centre study, Journal of Mental Health, 11, 223-230, 2002	Study design – no comparative cost analysis
Kapur, N., House, A., May, C., Creed, F., Service provision and outcome for deliberate self-poisoning in adults - Results from a six centre descriptive study, Social Psychiatry and Psychiatric Epidemiology, 38, 390-395, 2003	Study design – no comparative cost analysis
Kinchin, I., Russell, A. M. T., Byrnes, J., McCalman, J., Doran, C. M., Hunter, E., The cost of hospitalisation for youth self-harm:	Study design – no comparative cost analysis

Study	Reason for Exclusion
differences across age groups, sex, Indigenous and non-Indigenous populations, Social Psychiatry and Psychiatric Epidemiology, 55, 425-434, 2020	
O'Leary, F. M., Lo, M. C. I., Schreuder, F. B., "Cuts are costly": A review of deliberate self-harm admissions to a district general hospital plastic surgery department over a 12-month period, Journal of Plastic, Reconstructive and Aesthetic Surgery, 67, e109-e110, 2014	Study design – no comparative cost analysis
Olfson, M., Gameroff, M. J., Marcus, S. C., Greenberg, T., Shaffer, D., National trends in hospitalization of youth with intentional self-inflicted injuries, American Journal of Psychiatry, 162, 1328-1335, 2005	Study design – no comparative cost analysis
Ostertag, L., Golay, P., Dorogi, Y., Brovelli, S., Cromec, I., Edan, A., Barbe, R., Saillant, S., Michaud, L., Self-harm in French-speaking Switzerland: A socio-economic analysis (7316), Swiss Archives of Neurology, Psychiatry and Psychotherapy, 70 (Supplement 8), 48S, 2019	Conference abstract
Ougrin, D., Corrigall, R., Poole, J., Zundel, T., Sarhane, M., Slater, V., Stahl, D., Reavey, P., Byford, S., Heslin, M., Ivens, J., Crommelin, M., Abdulla, Z., Hayes, D., Middleton, K., Nnadi, B., Taylor, E., Comparison of effectiveness and cost-effectiveness of an intensive community supported discharge service versus treatment as usual for adolescents with psychiatric emergencies: a randomised controlled trial, The Lancet Psychiatry, 5, 477-485, 2018	Not self-harm. In addition, the interventions evaluated in this economic analysis (a supported discharge service provided by an intensive community treatment team compared to usual care) were not relevant to any review questions
Palmer, S., Davidson, K., Tyrer, P., Gumley, A., Tata, P., Norrie, J., Murray, H., Seivewright, H., The cost-effectiveness of cognitive behavior therapy for borderline personality disorder: results from the BOSCOT trial, Journal of Personality Disorders, 20, 466-481, 2006	Not self-harm
Quinlivan L, Steeg S, Elvidge J, et al. Risk assessment scales to predict risk of hospital treated repeat self-harm: A cost-effectiveness modelling analysis. J Affect Disord. 2019;249:208-215.	Not relevant to any of the review questions in the guideline - this study estimated the cost-effectiveness of of risk assessment scales versus clinical assessment for adults attending an emergency department following self-harm
Richardson JS, Mark TL, McKeon R. The return on investment of postdischarge follow-up calls for suicidal ideation or deliberate self-harm. Psychiatr Serv. 2014;65(8):1012-1019.	Not enough data reporting on cost-effectiveness findings
Smits, M. L., Feenstra, D. J., Eeren, H. V., Bales, D. L., Laurenssen, E. M. P., Blankers, M., Soons, M. B. J., Dekker, J. J. M., Lucas, Z., Verheul, R., Luyten, P., Day hospital versus intensive out-patient mentalisation-based treatment for borderline personality disorder: Multicentre randomised clinical trial, British Journal of Psychiatry, 216, 79-84, 2020	Not self-harm
Tsiachristas, A., Geulayov, G., Casey, D., Ness, J., Waters, K., Clements, C., Kapur, N., McDaid, D., Brand, F., Hawton, K., Incidence and general	Study design – no comparative cost analysis

Study	Reason for Exclusion
hospital costs of self-harm across England: estimates based on the multicentre study of self-harm, Epidemiology & Psychiatric Science, 29, e108, 2020	
Tsiachristas, A., McDaid, D., Casey, D., Brand, F., Leal, J., Park, A. L., Geulayov, G., Hawton, K., General hospital costs in England of medical and psychiatric care for patients who self-harm: a retrospective analysis, The Lancet Psychiatry, 4, 759-767, 2017	Study design – no comparative cost analysis
Tubeuf, S., Saloniki, E. C., Cottrell, D., Parental Health Spillover in Cost-Effectiveness Analysis: Evidence from Self-Harming Adolescents in England, PharmacoEconomics, 37, 513-530, 2019	This study is not a separate study from one already included in the guideline for topic 5.2 (Cottrel 2018). This secondary analysis presents alternative parental health spillover quantification methods in the context of a randomised controlled trial comparing family therapy with treatment as usual as an intervention for self-harming adolescents of (Cottrel 2018), and discusses the practical limitations of those methods
Tyrer, P., Thompson, S., Schmidt, U., Jones, V., Knapp, M., Davidson, K., Catalan, J., Airlie, J., Baxter, S., Byford, S., Byrne, G., Cameron, S., Caplan, R., Cooper, S., Ferguson, B., Freeman, C., Frost, S., Godley, J., Greenshields, J., Henderson, J., Holden, N., Keech, P., Kim, L., Logan, K., Manley, C., MacLeod, A., Murphy, R., Patience, L., Ramsay, L., De Munroz, S., Scott, J., Seivewright, H., Sivakumar, K., Tata, P., Thornton, S., Ukoumunne, O. C., Wessely, S., Randomized controlled trial of brief cognitive behaviour therapy versus treatment as usual in recurrent deliberate self-harm: The POPMACT study, Psychological medicine, 33, 969-976, 2003	Study design - no economic evaluation
Van Roijen, L. H., Sinnaeve, R., Bouwmans, C., Van Den Bosch, L., Cost-effectiveness and Cost-utility of Shortterm Inpatient Dialectical Behavior Therapy for Chronically Parasuicidal BPD (Young) Adults, Journal of Mental Health Policy and Economics, 18, S19-S20, 2015	Conference abstract
van Spijker, B. A., Majo, M. C., Smit, F., van Straten, A., Kerkhof, A. J., Reducing suicidal ideation: cost-effectiveness analysis of a randomized controlled trial of unguided web-based self-help, Journal of medical Internet research, 14, e141, 2012	Not self-harm

Appendix K Research recommendations – full details

Research recommendations for review question: What pharmacological interventions are effective for people who have self-harmed?

No research recommendations were made for this review question.