First aid interventions by laypeople for acute oral poisoning (Review)

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[Intervention Review]

First aid interventions by laypeople for acute oral poisoning

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ABSTRACT

Background

Oral poisoning is a major cause of mortality and disability worldwide, with estimates of over 100,000 deaths due to unintentional poisoning each year and an overrepresentation of children below five years of age. Any effective intervention that laypeople can apply to limit or delay uptake or to evacuate, dilute or neutralize the poison before professional help arrives may limit toxicity and save lives.

Objectives

To assess the effects of pre-hospital interventions (alone or in combination) for treating acute oral poisoning, available to and feasible for laypeople before the arrival of professional help.

Search methods

We searched the Cochrane Central Register of Controlled Trials, MEDLINE, Embase, CINAHL, ISI Web of Science, International Pharmaceutical Abstracts, and three clinical trials registries to 4 December 2018, and we also carried out reference checking and citation searching.

Selection criteria

We included randomized controlled trials comparing interventions (alone or in combination) that are feasible in a pre-hospital setting for treating acute oral poisoning patients, including but potentially not limited to activated charcoal (AC), emetics, cathartics, diluents, neutralizing agents and body positioning.

Data collection and analysis

Two review authors independently performed study selection, data collection and assessment. Primary outcomes of this review were incidence of mortality and adverse events, plus incidence and severity of symptoms of poisoning. Secondary outcomes were duration of symptoms of poisoning, drug absorption, and incidence of hospitalization and ICU admission.

Main results

We included 24 trials involving 7099 participants. Using the Cochrane 'Risk of bias' tool, we assessed no study as being at low risk of bias for all domains. Many studies were poorly reported, so the risk of selection and detection biases were often unclear. Most studies reported important outcomes incompletely, and we judged them to be at high risk of reporting bias.

All but one study enrolled oral poisoning patients in an emergency department; the remaining study was conducted in a pre-hospital setting. Fourteen studies included multiple toxic syndromes or did not specify, while the other studies specifically investigated paracetamol

(2 studies), carbamazepine (2 studies), tricyclic antidepressant (2 studies), yellow oleander (2 studies), benzodiazepine (1 study), or toxic berry intoxication (1 study). Twenty-one trials investigated the effects of activated charcoal (AC), administered as a single dose (SDAC) or in multiple doses (MDAC), alone or in combination with other first aid interventions (a cathartic) and/or hospital treatments. Six studies investigated syrup of ipecac plus other first aid interventions (SDAC + cathartic) versus ipecac alone. The collected evidence was mostly of low to very low certainty, often downgraded for indirectness, risk of bias or imprecision due to low numbers of events.

First aid interventions that limit or delay the absorption of the poison in the body

We are uncertain about the effect of SDAC compared to no intervention on the incidence of adverse events in general (zero events in both treatment groups; 1 study, 451 participants) or vomiting specifically (Peto odds ratio (OR) 4.17, 95% confidence interval (CI) 0.30 to 57.26, 1 study, 25 participants), ICU admission (Peto OR 7.77, 95% CI 0.15 to 391.93, 1 study, 451 participants) and clinical deterioration (zero events in both treatment groups; 1 study, 451 participants) in participants with mixed types or paracetamol poisoning, as all evidence for these outcomes was of very low certainty. No studies assessed SDAC for mortality, duration of symptoms, drug absorption or hospitalization.

Only one study compared SDAC to syrup of ipecac in participants with mixed types of poisoning, providing very low-certainty evidence. Therefore we are uncertain about the effects on Glasgow Coma Scale scores (mean difference (MD) −0.15, 95% CI −0.43 to 0.13, 1 study, 34 participants) or incidence of adverse events (risk ratio (RR) 1.24, 95% CI 0.26 to 5.83, 1 study, 34 participants). No information was available concerning mortality, duration of symptoms, drug absorption, hospitalization or ICU admission.

This review also considered the added value of SDAC or MDAC to hospital interventions, which mostly included gastric lavage. No included studies investigated the use of body positioning in oral poisoning patients.

First aid interventions that evacuate the poison from the gastrointestinal tract

We found one study comparing ipecac versus no intervention in toxic berry ingestion in a pre-hospital setting. Low-certainty evidence suggests there may be an increase in the incidence of adverse events, but the study did not report incidence of mortality, incidence or duration of symptoms of poisoning, drug absorption, hospitalization or ICU admission (103 participants).

In addition, we also considered the added value of syrup of ipecac to SDAC plus a cathartic and the added value of a cathartic to SDAC.

No studies used cathartics as an individual intervention.

First aid interventions that neutralize or dilute the poison

No included studies investigated the neutralization or dilution of the poison in oral poisoning patients.

Authors' conclusions

The studies included in this review provided mostly low- or very low-certainty evidence about the use of first aid interventions for acute oral poisoning. A key limitation was the fact that only one included study actually took place in a pre-hospital setting, which undermines our confidence in the applicability of these results to this setting. Thus, the amount of evidence collected was insufficient to draw any conclusions.

P L A I N   L A N G U A G E   S U M M A R Y

First aid treatments for oral poisoning

Review question

We reviewed the evidence on the effects of first aid treatments for poisoning that could be feasibly given by people who are not health professionals.

Background

Many first aid treatments are recommended for treating people who have ingested poisonous substances. Some treatments, such as activated charcoal (AC), bind to the poison, limiting the body's absorption of it. Others may induce vomiting (such as syrup of ipecac) or dilute or neutralize the poison (such as drinking water, milk or juices). Adjusting the person's body position may also have an effect.

Study characteristics

In December 2018 we searched for high-quality studies (randomly dividing participants into different treatment groups) investigating treatments for poisoning that laypeople can perform. We found 24 studies with 7099 participants. All but one study took place in hospitals; the remaining one was in a home setting.

Fourteen studies either did not specify the type of poison or studied different kinds. The others investigated overdoses of specific medicines (paracetamol, carbamazepine, antidepressant, benzodiazepine) or poisonous plants (yellow oleander or poisonous berries).

Twenty-one trials studied different treatments with activated charcoal: as a single dose or multiple doses, with or without other first aid treatments (a substance to speed up bowel transit), and with or without hospital treatments. Six studies compared syrup of ipecac, with or without other first aid treatments (single-dose activated charcoal plus bowel transit enhancing substance) versus no treatment. We found no studies that investigated the neutralization or dilution of the poison or the use of certain body positions.

Key results

Two studies compared a single dose of activated charcoal to no treatment following poisoning with paracetamol or different kinds of poisoning. We are uncertain about the treatment's side effects, admission to intensive care or worsening of the patient, and there was no information about effects on death, symptom duration, poison uptake or hospitalization.

One study compared a single dose of activated charcoal to ipecac in mixed types of poisoning. We are uncertain about the effect of activated charcoal compared to ipecac, on the patient's level of coma or the number of unwanted effects. There was no information about effects on death, symptom duration, poison uptake, hospitalization or intensive care admission.

One study compared ipecac to no treatment in children who ate poisonous berries at home. There may be an increase in the number of unwanted effects for ipecac. There was no information about effects on death, poisoning symptoms, symptoms duration, poison uptake, hospitalization or intensive care admission.

We also investigated the use of single-dose or multi-dose activated charcoal, with or without hospital treatment, compared to each other or no treatment. Furthermore, we investigated the added value of ipecac to single-dose activated charcoal and the added value of adding bowel transit enhancing substances to AC.

Certainty of the evidence

All but one study took place in a hospital setting, which means that the results cannot be directly applied to the lay setting. Because studies did not always report the methods they used, we are uncertain about the quality of the research conduct for many. Outcomes important to patients and pre-specified by us as important outcomes for this review were often absent or incompletely reported. Our certainty about the results of this review is mostly low to very low. Therefore future research is highly likely to change the findings.

Conclusion

Based on the identified evidence, we cannot draw any conclusions about the effects of any of the investigated first aid treatments in a lay setting.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.   SDAC versus no intervention for first aid in patients with acute oral poisoning

SDAC versus no intervention for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (paracetamol or not specified)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC)
Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	**Risk with SDAC**				
Incidence of mortality	No studies collected or reported this outcome					
Incidence of adverse events	Control group: 0/236; intervention group: 4/240 (Peto OR 4.17, 95% CI 0.30 to 57.26)		—	476 (2 RCTs)	⊕⊝⊝⊝ Very low[a,b,c]	We are uncertain of the effect of SDAC on the incidence of adverse events.
Incidence and severity of symptoms of poisoning: incidence of clinical deterioration during stay in the hospital	—		—	451 (1 RCT)	⊕⊝⊝⊝ Very low[a,b,d]	The relative effect was not estimable due to the absence of events in the intervention (0/220) and the control group (0/231). We are uncertain of the effect of SDAC on incidence and severity on poisoning.
Duration of toxic symptoms	No studies collected or reported this outcome					
Drug absorption	No studies collected or reported this outcome					
Incidence of hospitalization	No studies collected or reported this outcome					
Incidence of ICU admission	Control group: 0/231; intervention group: 1/220 (Peto OR 7.77, 95% CI 0.15 to 391.93)		—	451 (1 RCT)	⊕⊝⊝⊝ Very low[a,b,c]	We are uncertain of the effect of SDAC on the incidence of ICU admission.

The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **ICU**: intensive care unit; **MD**: mean difference; **RCT**: randomized controlled trial; **RR**: risk ratio; **SDAC**: single-dose activated charcoal; **OR**: odds ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious limitations in study design: high risk of selection bias.
[b]Downgraded one level for serious indirectness: study conducted in a hospital setting.
[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.
[d]Downgraded one level for serious imprecision: low number of events.

Summary of findings 2.   SDAC + hospital intervention versus hospital intervention alone for first aid in patients with acute oral poisoning

SDAC + hospital intervention versus hospital intervention alone for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (not specified, tricyclic antidepressants, combinations of different drugs or yellow oleander)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC) + hospital intervention
Comparison: hospital intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of partici-pants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hospital in-tervention	**Risk with SDAC + hospi-tal intervention**				
Incidence of mortality	Study population		Peto OR 1.04 (0.79 to 1.37)	3425 (2 RCTs)	⊕⊕⊝⊝ Low[a,b]	SDAC in addition to hospital treatments may make little or no difference on inci-dence of mortality.
	62 per 1000	64 per 1000 (49 to 85)				
Incidence of ad-verse events	Incidence of vomiting: intervention group: 118/570 and control group: 163/1236 (RR 1.44, 95% CI 0.88 to 2.37; 1806 participants; 2 studies). Incidence of absent bowel sounds: intervention group: 7/1544 and control group: 17/1554 (RR 0.41, 95% CI 0.17 to 1.00, 1 study, 3098 participants).		—	4904 (3 RCTs)	⊕⊝⊝⊝ Very low[a,c,d]	Statistically significant heterogeneity was found, which may be explained par-tially by subgroup analyses per type of adverse event. We are uncertain about the effect of SDAC in addition to hospital treatments on incidence of adverse events.
Incidence and severity of symptoms of poisoning: inci-	Patients that received gastric lavage prior to SDAC: intervention group: 80/1578 and control group: 87/1597 (RR 0.95, 95% CI 0.70 to 1.27, 2 studies, 3175 participants).		—	3562 (4 RCTs)	⊕⊝⊝⊝ Very low[a,b,c]	Statistically significant heterogeneity was found, which may be explained by subgroup analyses in patients receiving or not receiving gastric lavage.

dence of need for intubation	Patients that did not receive gastric lavage prior to SDAC: intervention group: 24/194 and control group: 10/193 (RR 2.61, 95% CI 1.38 to 4.93, 1 study, 387 participants).					We are uncertain about the effect of SDAC on incidence of need for intubation.
Duration of toxic symptoms: duration of intubation (h)	Eddleston 2008: intervention group median (IQR): 112.0 (36.6 to 234.9) h and control group median (IQR): 88.5 (38.5 to 203.1) h (median difference: 23.5 h, P > 0.05). Merigian 2002: intervention group mean: 54.6 h and control group mean: 39.9 h (MD: 14.7 h, P = 0.70).		—	(2 RCTs)	⊕⊕⊝⊝ Low[a,e]	Data were reported as median with IQR in one or means without measure of spread in another study, without information on participant numbers. SDAC in addition to hospital treatments may make little or no difference on the duration of intubation.
Drug absorption: cardenolide: AUC (μg/L) × h Follow-up: 1 days	The median (IQR) in intervention group was 17.7 (11.1 to 21.8) (μg/L) × h and in the control group 19.0 (13.7 to 24.3) (μg/L) × h (median difference: −1.3 h, P > 0.05)		—	68 (1 RCT)	⊕⊝⊝⊝ Very low[a,f,g]	We are uncertain about the effect of SDAC in addition to hospital treatments on cardenolide absorption.
Incidence of hospitalization	125 per 1000	196 per 1000 (152 to 252)	RR 1.57 (1.22 to 2.02)	1479 (1 RCT)	⊕⊝⊝⊝ Very low[a,g,h]	We are uncertain about the effect of SDAC in addition to hospital treatments on incidence of hospitalization.
Incidence of ICU admission	30 per 1000	69 per 1000 (42 to 114)	RR 2.33 (1.42 to 3.82)	1479 (1 RCT)	⊕⊝⊝⊝ Very low[a,g,h]	We are uncertain about the effect of SDAC in addition to hospital treatments on incidence of ICU admission.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; ICU: intensive care unit; IQR: interquartile range; RCT: randomized controlled trial; RR: risk ratio; SDAC: single-dose activated charcoal; OR: odds ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious indirectness: study conducted in a hospital setting.

[b]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

[c]Downgraded one level for serious inconsistency: large and statistically significant heterogeneity present (I² > 60%, P < 0.10).

[d]Downgraded one level for serious imprecision: wide confidence intervals.

[e]Downgraded one level for serious imprecision: lack of data on the number of patients analysed.

[f]Downgraded one level due to serious limitations in study design: high risk of other bias: it is not entirely clear what is measured with the assay used. The fact that both active cardenolides and (inactive) metabolites might be detected by the assay compromise the results of these analyses, as they might explain the wide variability observed.

[g]Downgraded one level for serious imprecision: low number of events.

[h]Downgraded one level for serious limitations in study design: high risk of selection bias.

Summary of findings 3.   MDAC + hospital intervention versus SDAC + hospital intervention for first aid in patients with acute oral poisoning

MDAC + hospital intervention versus SDAC + hospital intervention for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (carbamazepine, yellow oleander, or combinations of different drugs)
Setting: hospital setting
Intervention: multiple dose of activated charcoal (MDAC) + hospital intervention
Comparison: single-dose activated charcoal (SDAC) + hospital intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of partici-pants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with SDAC + hospital intervention	Risk with MDAC + hospital intervention				
Incidence of mortality	Study population		RR 0.59 (0.21 to 1.63)	3476 (2 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	Combining the studies resulted in statistically significant heterogeneity, for which explanations remain speculative.
	72 per 1000	42 per 1000 (15 to 117)				We are uncertain about the effects of MDAC in addition to hospital treatment, compared to SDAC, in addition to hospital treatment.
Incidence of adverse events	Study population		Peto OR 3.55 (1.85 to 6.79)	3476 (2 RCTs)	⊕⊕⊖⊖ Low[b,c]	There was statistically significant heterogeneity, which may be attributable to different adverse events measured in individual studies.
	4 per 1000	14 per 1000 (7 to 27)				MDAC in addition to hospital treatment may increase abdominal discomfort/diarrhoea and absent bowel sounds, compared to SDAC in addition to hospital treatment.
Incidence and severity of symptoms of poisoning: incidence of need for intubation	Study population		RR 1.01 (0.75 to 1.38)	3097 (2 RCTs)	⊕⊕⊖⊖ Low[b,c]	MDAC in addition to hospital treatment may make little or no difference in the incidence of need for intubation, compared to SDAC in addition to hospital treatment.
	49 per 1000	49 per 1000 (37 to 67)				

Duration of toxic symptoms: duration of intubation (h)	Brahmi 2006: intervention group: 24.1 (SD 4.2 h and control group 36.4 (SD 3.6 h (MD: 12.30 h lower, 95% CI −18.56 to −6.04, 6 participants). Eddleston 2008: intervention group median (IQR): 83.8 (35.0 to 173.0) h and control group median (IQR): 112.0 (36.6 to 234.9) h (median difference: 28.2 h), unclear number of participants	—	(2 RCTs)	⊕⊖⊖⊖ Very low[b,d,e]	Data were reported as means with SD in one study or medians with IQR in another study, without information on participant numbers or statement of significance. We are uncertain about the effects of MDAC in addition to hospital treatment on duration of intubation, compared to SDAC in addition to hospital treatment.
Drug absorption: cardenolide: AUC (μg × L/h) Follow-up: 1 days	The median (IQR) in intervention group was 17.3 (12.8 to 21.7) (μg/L) × h and in the control group 17.7 (11.1 to 21.8) (μg/L) × h (median difference −0.4, P > 0.05).	—	64 (1 RCT)	⊕⊖⊖⊖ Very low[b,e,f]	We are uncertain about the effects of MDAC in addition to hospital treatment on cardenolide drug absorption, compared to SDAC in addition to hospital treatment.
Incidence of hospitalization	No studies collected or reported this outcome				
Incidence of ICU admission	Study population 80 per 1000 25 per 1000 (10 to 66)	RR 0.31 (0.12 to 0.83)	401 (1 RCT)	⊕⊕⊖⊖ Low[b,g]	MDAC in addition to hospital treatment may result in a decreased incidence of ICU admission, compared to SDAC in addition to hospital treatment.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

AUC: area under the receiver operating curve; CI: confidence interval; ICU: intensive care unit; IQR: interquartile range; MDAC: multi-dose activated charcoal; RCT: randomized controlled trial; RR: risk ratio; SD: standard deviation; SDAC: single-dose activated charcoal; OR: odds ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious inconsistency: combining results resulted in a considerable and statistically significant degree of heterogeneity (I² > 60%, P < 0.10).

[b]Downgraded one level for serious indirectness: study conducted in a hospital setting.

[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

[d]Downgraded one level for other limitations: inconsistent conclusions made by the studies.

[e]Downgraded one level for serious imprecision: low sample size and lack of data.

[f]Downgraded one level for serious study limitations: high risk of other bias: it is not entirely clear what is measured with the assay used. The fact that both active cardenolides and (inactive) metabolites might be detected by the assay compromise the results of these analyses, as they might explain the wide variability observed.
[g]Downgraded one level for serious imprecision: low number of events.

Summary of findings 4.   SDAC versus syrup of ipecac for first aid in patients with acute oral poisoning

SDAC versus syrup of ipecac for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (anti-inflammatory drugs, analgesics or psychotropic drugs)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC)
Comparison: syrup of ipecac

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with syrup of ipecac	**Risk with SDAC**				
Incidence of mortality	No studies collected this outcome					
Incidence of adverse events	Study population		RR 1.24 (0.26 to 5.83)	34 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,c]	We are uncertain about the effect of SDAC, compared to syrup of ipecac on incidence of adverse events.
	154 per 1000	191 per 1000 (40 to 897)				
Incidence and severity of symptoms of poisoning: level of coma assessed with Glasgow Coma Scale Scale from: 3 to 15 Follow-up: 1 h	The mean incidence and severity of symptoms of poisoning: level of coma was 14.91	MD 0.15 lower (0.43 lower to 0.13 higher)	—	34 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,d]	We are uncertain about the effect of SDAC, compared to syrup of ipecac on the level of coma.
Duration of toxic symptoms	No studies collected this outcome					
Drug absorption	No studies collected this outcome					
Incidence of hospitalization	No studies collected this outcome					
Incidence of ICU admission	No studies collected this outcome					

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **ICU**: intensive care unit; **MD**: mean difference; **RCT**: randomized controlled trial; **RR**: risk ratio; **SDAC**: single-dose activated charcoal.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious study limitations: high risk of selection bias.

[b]Downgraded one level for serious indirectness: study conducted in a hospital setting.

[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

[d]Downgraded one level for serious imprecision: low sample size.

Summary of findings 5.   MDAC + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning

MDAC + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (benzodiazepines, yellow oleander or combinations of different drugs)
Setting: hospital setting
Intervention: multi-dose activated charcoal (MDAC) + hospital intervention
Comparison: hospital intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hospital intervention	**Risk with MDAC + hospital intervention**				
Incidence of mortality	Study population		RR 0.94 (0.72 to 1.22)	3085 (1 RCT)	⊕⊕⊖⊖ Low[a,b]	MDAC in addition to hospital treatment may make little or no difference in incidence of mortality.
	68 per 1000	64 per 1000 (49 to 82)				
Incidence of adverse events	Study population		RR 1.02 (0.52 to 1.98)	3085 (1 RCT)	⊕⊕⊖⊖ Low[a,b]	MDAC in addition to hospital treatment may make little or no difference in incidence of adverse events.
	11 per 1000	11 per 1000 (6 to 22)				
Incidence and severity of symptoms of poisoning: incidence of need for intubation	Study population		RR 0.97 (0.71 to 1.33)	3085 (1 RCT)	⊕⊕⊖⊖ Low[a,b]	MDAC in addition to hospital treatment may make little or no difference in incidence of need for intubation.
	49 per 1000	47 per 1000 (35 to 65)				

Duration of toxic symptoms: length of intubation (h)	The median (IQR) length of intubation in the intervention group was 83.8 (35.0 to 173.0) h and 88.5 (38.5 to 203.1) h in the control group and was reported not to differ significantly (P > 0.05); unclear number of participants	—	(1 RCT)	⊕⊕⊖⊖ Low[a,c]	The number of participants analysed was not reported. MDAC in addition to hospital treatment may make little or no difference in length of intubation
Drug absorption: cardenolide: AUC (µg/L × h) Follow-up: 1 day	The median (IQR) cardenolide AUC in the intervention group was 17.3 (12.8 to 21.7) (µg/L) × h and 19.0 (13.7 to 24.3) (µg/L) × h in the control group.	—	76 (1 RCT)	⊕⊖⊖⊖ Very low[a,c,d]	We are uncertain about the effects of MDAC in addition to hospital treatment on cardenolide drug absorption.
Incidence of hospitalization	No studies collected or reported this outcome				
Incidence of ICU admission	No studies collected or reported this outcome				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AUC: area under the receiver operating curve; **CI**: confidence interval; **ICU**: intensive care unit; **IQR**: interquartile range; **MDAC**: multi-dose activated charcoal; **RCT**: randomized controlled trial; **RR**: risk ratio.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious indirectness: study conducted in a hospital setting.
[b]Downgraded one level for serious imprecision: low number of events and wide confidence interval.
[c]Downgraded one level for serious imprecision: low sample size and lack of data.
[d]Downgraded one level for serious study limitations: high risk of other bias: it is not entirely clear what is measured with the assay used. The fact that both active cardenolides and (inactive) metabolites might be detected by the assay compromise the results of these analyses, as they might explain the wide variability observed.

Summary of findings 6.   Syrup of ipecac versus no intervention for first aid in patients with acute oral poisoning

Syrup of ipecac versus no intervention for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (toxic berries)
Setting: pre-hospital setting
Intervention: syrup of ipecac

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of partici-pants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	**Risk with Syrup of ipecac**				
Incidence of mortality	No studies collected this outcome					
Incidence of adverse events: diarrhoea Follow-up: 1 day	Study population		RR 4.08 (1.66 to 10.04)	103 (1 RCT)	⊕⊕⊝⊝ Low[a,b]	Syrup of ipecac may result in an increased incidence of diarrhoea.
	96 per 1000	392 per 1000 (160 to 965)				
Incidence and severity of symptoms of poisoning	No studies collected this outcome					
Duration of toxic symptoms	No studies collected this outcome					
Drug absorption	No studies collected this outcome					
Hospitalization: incidence of hospital-ization Follow-up: 1 days	—		—	103 (1 RCT)	⊕⊕⊝⊝ Low[a,b]	The effect was not estimable due to the absence of events in the in-tervention (0/52) and the control group (0/51).
ICU admission	No studies collected this outcome					

The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **ICU**: intensive care unit; **RCT**: randomized controlled trial; **RR**: risk ratio.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for serious study limitations: high risk of selection bias, high risk of detection bias, and high risk of other bias (no confirmation of actual ingestion or uptake, reporting of dichotomous outcomes while measuring with an ordinal scale).
[b]Downgraded one level for serious imprecision: low number of events.

BACKGROUND

Description of the condition

Poisoning can be defined as exposure of the body to exogenous substances, in sufficiently large amounts to cause harm to the individual. This can happen through chronic exposure to low doses of a substance, or more acutely through sudden exposure to a harmful dose. Acute poisoning can happen either accidentally or voluntarily, as a way to end one's own or another's life or as a 'cry for help'.

Poisoning inflicts a major burden of morbidity and mortality worldwide. The World Health Organization (WHO) estimates that 108,000 deaths a year are caused by unintentional poisoning (WHO 2016), accompanied by the loss of a staggering 6,558,000 disability adjusted life years (DALYs) (WHO 2016). In addition to this, auto-intoxication is one of the most common methods to attempt suicide. Yearly, around 800,000 people worldwide commit suicide, and around 30% of their attempts occur through the intake of pesticides, a phenomenon typically occurring in rural areas in lower- and middle-income countries (WHO 2018). As most attempted suicides are unsuccessful, the actual burden will be much higher (Albert 2015). Poisoning can happen via different routes of exposure, such as through inhalation, injection or dermal absorption, but by far the most common is through deliberate or accidental ingestion of a toxic substance (Mowry 2016), which is the focus of this review. An important patient group to suffer from unintentional poisoning are young children. Roughly 20% of all accidental poisonings are thought to occur in children aged under 5 years (WHO 2016). In high-income countries, this proportion is even larger: up to 47% of the incoming calls to the American Poison Control Centers concern exposures in this age group (Mowry 2016). This is most likely because young children are curious to explore their environment and do not realize the dangers of putting unknown and potentially harmful things in their mouth. Indeed, large numbers of exposures are to cosmetics and household products (25% of all reported exposures in children aged 5 years or younger; Mowry 2016).

Hospital treatment of acute oral poisoning focuses initially on supportive therapy: hypertonic glucose infusion, maintaining the victim's vital parameters and keeping poison-induced symptoms under control (Isbister 2016; Nelson 2011). If practitioners can identify a toxin syndrome, they can administer a poison-specific antidote, for example N-acetylcysteine for a paracetamol overdose or naloxone for an opioid overdose (Chiew 2018; Wilkerson 2016). Third-line treatment options include gastrointestinal decontamination procedures: activated charcoal can adsorb the poisonous substance (Corcoran 2016), while gastric lavage or whole bowel irrigation are procedures that attempt to eliminate the poison out of the gastrointestinal tract before absorption into the blood (Donkor 2016; Thanacoody 2015). A final treatment strategy is to eliminate toxins that have already been absorbed through multiple doses of activated charcoal, haemodialysis or blood/urinary alkalinization (Decker 2015; Gaudreault 2005; Proudfoot 2003; Roberts 2005).

In cases of acute oral poisoning, a swift reaction is crucial. For activated charcoal (AC), experimental studies have shown that its efficacy in limiting drug absorption decreases dramatically over time (Chyka 2005). Therefore, treatment guidelines recommend using AC within an hour after ingestion of the poison, although AC may still produce effects after that time, especially in drugs administered in a delayed release formula (Chyka 2005; Juurlink 2015). However, it is difficult to adhere to these guidelines in emergency services, mainly due to the delay between ingestion and presentation at the emergency department (Karim 2001; LoVecchio 2007; Tuuri 2009). Thus, any effective first aid measure that would neutralize, limit or delay uptake, or promote evacuation from the gastrointestinal tract in case of acute oral poisoning, could save precious time for professionals, potentially making the difference between life and death, or serious morbidity, for the poisoned patient.

First aid, as defined by the International Liaison Committee On Resuscitation (ILCOR), is the immediate help provided to a sick and injured person until professional help arrives. First aid interventions seek to preserve life, alleviate suffering, prevent further illness or injury and promote recovery (Zideman 2015). This definition implies that a first aid intervention must be both available to and feasible for a layperson in a pre-hospital setting. Of the previously mentioned hospital interventions, only activated charcoal, which is relatively easy to administer orally and available without prescription, is feasible. In addition to these, other suggested first aid techniques include administering emetics, such as syrup of ipecac (or ipecacuanha) (Quang 2000); using cathartics, such as sorbitol (Keller 1990), drinking water, milk, vinegar or citrus juice to dilute and/or neutralize the poison (Rumack 1977); or adjusting the poisoned victim's body position to slow down the uptake of the poison (Vance 1992).

In case of ingestion of toxic alcohols (e.g. methanol, ethylene glycol), ethanol could be considered a potential home remedy due to its wide availability. However, the use of large volumes of ethanol is dangerous and needs to be monitored carefully (Rietjens 2014). Therefore, it is not recommended for use in a lay setting without professional guidance. Current recommendations for laypeople are limited to placing the victim in the lateral decubitus position and seeking professional help (e.g. contacting poison control centres if available) and following their advice (IFRC 2016).

Description of the intervention

The focus of this Cochrane Review is any intervention that is readily available to and administrable by laypeople before professional help arrives, targeted at neutralizing, limiting or delaying the absorption, or promoting the evacuation of a poison.

Limiting the absorption of a poison can be achieved by administering an adsorbent, such as activated charcoal. This black powder is produced through pyrolysis of carbon-rich materials and activation by steam to remove already adsorbed substances (Olson 2010). This process results in a material with a very large surface area and hence adsorbing capacity. It needs to be mixed with water to form a slurry that can be ingested.

Placing the poisoning victim on their left side might be another method to decrease absorption of the poison (Vance 1992).

Substances that can promote the evacuation of a poison from the gastrointestinal tract firstly include emetics. The best known and most recommended is syrup of ipecacuanha, or ipecac. This syrup is derived from the roots and rhizome of *Cephaelis ipecacuanha* (Lee 2008). Other suggested emetics are apomorphine and copper sulphate. Apomorphine is believed to induce vomiting faster than

ipecac (MacLean 1973), but it is not feasible to administer in a home setting and can cause central nervous depression, so it is not recommended, especially in children (MacLean 1973). Copper sulphate has also been used to induce vomiting in people with oral poisoning due to its action as a local irritant in the stomach (Karlsson 1965). However, it is a common source of intoxication itself, hence its use is also discouraged (Nastoulis 2017).

A second class of substances that can theoretically speed up the evacuation of an ingested poison from the gastrointestinal tract are cathartics. Patients who have ingested slow-absorbing materials might benefit most from these treatments, although current guidelines suggest not using cathartics without activated charcoal (American Academy of Clinical Toxicology 2004). Examples of suggested cathartics include sugars, such as mannitol, lactulose and sorbitol, or salts, including magnesium sulphate, magnesium citrate and sodium sulphate.

In addition, diluting and neutralizing poisons, especially caustic substances such as lye, could occur through the intake of water, milk, vinegar or citrus juice (Rumack 1977). Milk might also have some adsorbing capacity (Chin 1969).

How the intervention might work

First aid interventions to treat poisoning can be categorized in four groups:

- those that either limit or delay absorption of the poison in the body, such as activated charcoal or certain body positions;
- interventions that evacuate the poison from the gastrointestinal tract, either by vomiting or by defecation;
- combinations of first aid interventions that limit uptake and promote evacuation of the poison, e.g. sorbitol and activated charcoal;
- first aid interventions that neutralize or dilute the poison, such as drinking water, milk, vinegar or citrus juice.

Furthermore, other combinations of first aid interventions may also be used.

A. First aid interventions that limit or delay the absorption of the poison in the body

One way to limit the absorption of a poison is to administer a substance that binds to the poison, thus preventing it from being absorbed by the body. Activated charcoal (AC) is one such adsorbent. Its enormous surface area can adsorb large quantities of drugs through the generation of Van der Waals forces between the charcoal and the adsorbed molecule (Olson 2010). Not all substances are equally effectively bound by AC. For example, lithium, iron, cyanide or alcohols bind to AC only to a minor extent, which means its appropriateness needs to be carefully considered in these cases (Bateman 1999; Juurlink 2015; Olson 2010). The optimal dose regimen for activated charcoal administration is not entirely clear, but 25 g to 100 g is considered to be a standard dose for adults (Chyka 2005). In practice, ingesting more than 50 g seems to be difficult to achieve for patients.

A certain body position might also slow down the uptake of the poison. The primary site of absorption for most pharmacologic substances is the small intestine, because of its large surface area and thin epithelium. Therefore, any factor that would delay gastric emptying into the small intestine should decrease the rate of absorption and limit the potential toxic effects of the ingested drug. Studies indicate that laying on the right side accelerates gastric emptying (Loots 2013; Valeur 2015; Van Wijk 2007). In contrast, placing the patient in the left lateral decubitus position might slow the rate of absorption of the ingested poison, because the anatomy of the stomach, combined with gravity, would allow the gastric content to stay in the greater curvature of the stomach (Vance 1992).

B. First aid interventions that evacuate the poison from the gastrointestinal tract

Evacuation of the poison from the gastrointestinal tract as quickly as possible can be achieved by inducing vomiting or accelerating defecation. Two types of drugs can be considered: emetics induce vomiting, while cathartics accelerate defecation.

As mentioned before, syrup of ipecac is the best known type of emetic. The main active substances of the ipecacuanha plant are emetine and cephaeline, which induce emesis and diarrhoea by acting both as a local irritant in the upper gastrointestinal tract and by targeting the chemoreceptor trigger zone in the medulla oblongata of the brain, the body's vomiting centre (Lee 2008). A potential risk associated with the use of emetics is lung injury through vomit aspiration (Höjer 2013).

Cathartics draw water into the large intestine, thereby stimulating bowel movements and thus accelerating defecation (American Academy of Clinical Toxicology 2004).

C. First aid interventions that limit uptake and promote evacuation of the poison from the gastrointestinal tract

Cathartics can be used with activated charcoal. This combination is thought to reduce drug uptake by accelerating evacuation out of the small bowel (Moon 2015). Furthermore, cathartics counteract the constipating effects of AC (James 1995). On the other hand, in vitro studies have suggested that cathartics might influence the adsorbing capacity of AC (Orisakwe 2001).

D. First aid interventions that neutralize or dilute the poison

A commonly used home remedy for poisoning by caustic substances is drinking large amounts of fluids, such as water, milk, vinegar or citrus juice (Rumack 1977). The rationale behind this is not only to dilute the poison, but also to change the pH in the stomach, thereby neutralizing the caustic effects of the ingested poison. Considerations that need to be made when using this approach are the chemical properties of the ingested substance (acidic or basic), the heat production that might occur during neutralization and sufficient availability of the neutralizing substance. In addition to its potential neutralizing effect, in vitro data suggest that milk has some adsorbing capacity (Chin 1969). However, increasing the volume of fluids in the stomach might also increase the rate of emptying into the small bowel, where the absorption of the poison takes place (Blain 2011). Furthermore, drinking large amounts of water might cause water intoxication (Lai 2016). A final consideration is that drinking large volumes of fluids might increase the risk of vomiting, which could be problematic in cases of caustic poisoning, as the caustic substance would contact the oesophagus for a second time.

Why it is important to do this review

There are several Cochrane Reviews concerning the treatment and prevention of poisoning. Kendrick 2012 provided evidence on interventions to prevent injuries at home, including cases of oral poisoning, while Hawton 2015 investigated potential interventions to decrease self-harm in children, adolescents and adults. A review by Nussbaumer-Streit 2016 documented potential household interventions to prevent domestic lead exposure in children. In addition, numerous Cochrane Reviews have investigated the use of hospital interventions to treat a range of specific intoxications, such as for example paracetamol or lithium poisoning (Chiew 2018; Lavonas 2015).

This Cochrane Review fills the gap between prevention and hospital treatment of poisoning, by investigating which pre-hospital interventions, available and feasible for a lay person in a non-healthcare setting, are effective in cases of acute oral poisoning. Identified interventions can be used in first aid guidelines targeted at lay people in settings such as nightclubs, childcare centres or the workplace, to be applied before arrival of professional help. As time is a crucial factor in acute oral poisoning, effective interventions conducted by laypeople would save valuable time and could therefore be crucial to survival (Chyka 2005; Juurlink 2015).

O B J E C T I V E S

To assess the effects of pre-hospital interventions (alone or in combination) for treating acute oral poisoning, available to and feasible for laypeople before the arrival of professional help.

M E T H O D S

Criteria for considering studies for this review

Types of studies

We considered randomized controlled trials (RCTs) in actual poisoning patients. We excluded studies involving healthy volunteers and preclinical studies (animal studies, in vitro research).

In order to be eligible for inclusion in the review, all RCTs taking place after 2010 must have been prospectively registered (Roberts 2015). All RCTs conducted prior to 2010 were eligible for inclusion.

Types of participants

We included participants poisoned via oral ingestion, both deliberately and accidentally. In addition to studies in a community setting, we considered studies conducted in a healthcare setting, including a hospital setting or ambulatory care, as most studies identified would likely have been performed in a controlled setting. Although this may be a source of indirectness, we feel that excluding these studies would result in selection bias.

Types of interventions

All identified first aid interventions, alone or in combination and feasible for a layperson in a pre-hospital setting, were eligible. These included, among others, activated charcoal and other adsorbents (single- or multi-dose); syrup of ipecac and other emetics (single or multi-dose); cathartics (single or multi-dose); body positioning; and water, milk, vinegar or citrus juice.

We compared the interventions to each other or to no intervention. We did not compare them to typical hospital interventions such as gastric lavage, whole bowel irrigation or the use of antidotes. However, if pre-hospital treatments were used in adjuvant to an established hospital treatment, we included these studies. The reason for not considering established hospital treatments as comparisons is that we are interested in the most efficacious treatments in a non-healthcare setting. It is likely that these would be less efficient than a hospital treatment, but they might still be useful as a first aid measure, which typically takes place before presentation to a healthcare facility.

Co-interventions were allowed if all groups received them in equal doses. We separately explored interventions aiming to limit or delay absorption of poison, evacuate poison, limit uptake and evacuate poison, and neutralize or dilute poison.

Types of outcome measures

Timings of outcomes are defined as early (within 24 h after poisoning), intermediate (24 h to one week after poisoning) and late (more than one week and less than one year after poisoning).

Primary outcomes

- Incidence of mortality
- Incidence of adverse events due to the intervention
- Incidence and severity of symptoms of poisoning, reported for example with the Poisoning Severity Score (PSS) (Persson 1998)

Secondary outcomes

- Duration of toxic symptoms
- Drug absorption: measured as maximal concentration of drug in the blood (C_{max}), time to C_{max} (T_{max}) or area under the curve (AUC) of drug concentration versus time
- Incidence of hospitalization
- Incidence of intensive care unit (ICU) admission

Search methods for identification of studies

Electronic searches

We searched the following databases on 4 December 2018, without any language restrictions or date limits.

- The Cochrane Library (2018, Issue 11, searched 4 December 2018; www.cochranelibrary.com), including the following databases.
  - * The *Cochrane Database of Systematic Reviews*.
  - * The Cochrane Central Register of Controlled Trials (CENTRAL), for reports of RCTs from MEDLINE, Embase and records submitted from Cochrane Specialized Registers, including the Cochrane Injuries Group.
  - * DARE (Database of Abstracts of Reviews of Effect).
- MEDLINE, using the PubMed interface (1966 to 4 December 2018).
- Embase, using the Embase.com interface (1947 to 4 December 2018).
- CINAHL, using the EBSCO host interface (1982 to 4 December 2018).

- ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) and Conference Proceedings Citation Index-Science (CPCI-S) (1900 to 4 December 2018).
- International Pharmaceutical Abstracts, using the Ovid interface (1970 to 4 December 2018).
- Clinicaltrials.gov (clinicaltrials.gov).
- EU Clinical Trials Register (www.clinicaltrialsregister.eu).
- WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/en/).

For each of the articles included, we did a search in MEDLINE (via the PubMed interface) and screened the first 20 similar articles for additional relevant publications. Search strategies can be found in Appendix 1. Furthermore, we searched previously published systematic reviews and evidence-based guidelines that were identified during the database searches (Table 1).

We included relevant conference abstracts retrieved from searches in the above-mentioned databases in the review.

Searching other resources

We searched the reference list of included articles, retrieved with the above searches, to identify other studies.

Data collection and analysis

Selection of studies

Two authors (BA and VB or AV) independently screened the titles and abstracts of all references yielded by the search. Subsequently, we retrieved full texts of selected articles, using a study selection form to assess eligibility. We resolved any discrepancies between authors through discussion. In cases where no consensus could be reached, we consulted a third author (EDB or AV). We documented the included studies in the appropriate sections within the review and summarized studies that were excluded after full-text assessment in the Characteristics of excluded studies table, together with the reason for exclusion. We describe identified studies that were selected based on study design, study population and intervention of interest, but which reported no outcome of interest or outcome data, in the Results section of the review. We tried to contact the authors to ascertain whether the data for our outcomes of interest were unavailable due to lack of measurement or lack of reporting.

Data extraction and management

Two authors (BA and VB or AV) independently extracted data from all studies using a standardized and piloted data extraction form.

They extracted the following information from each study.

- General information: author, year of publication, year of study, country of study lead author.
- Study characteristics.
  * Study design.
  * Information on study population: number of participants, age, sex, country of study and poisoning characteristics (type and dose of intoxication, deliberate or accidental intoxication, time elapsed between intoxication and intervention, experimental or community setting).

  * Details of the intervention and the comparison: type of intervention, dose, route of administration, duration of the treatment.
  * Outcome(s) measured.
- Study findings.
  * Effects of the intervention on the outcome: effect measure, confidence interval, P value.
  * Number of events and participants in intervention and comparison groups.

Assessment of risk of bias in included studies

Two authors (BA and VB or AV) independently assessed risk of bias in the included studies using Cochrane's 'Risk of bias' tool (Higgins 2011). They assessed the domains of sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data addressed, selective reporting and possible other bias, rating each domain as being at low, high or unclear risk of bias.

Measures of treatment effect

We used Review Manager 5 (RevMan 5) to manage data and conduct analyses (RevMan 2014). We reported continuous outcomes as mean differences (MD) with 95% confidence intervals (CIs) and dichotomous outcomes as risk ratios (RR) with 95% CIs, or Peto odds ratios (OR) when events were rare and criteria were satisfied.

Unit of analysis issues

We identified studies that had a multi-arm design. We were cautious during the analysis of these data, ensuring that the same group of participants was not included twice in the meta-analysis. We achieved this by ensuring that separate interventions were not included in a single meta-analysis. Secondly, if multiple doses or administration times of an intervention were compared to a control group, we combined groups to create a single pair-wise comparison in the case of dichotomous outcomes, according to the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions* on the analysis of multi-arm trials (Higgins 2011). We did not identify multi-arm trials reporting continuous outcomes.

Dealing with missing data

In case of missing data, we attempted to contact the authors to obtain these data at least twice, if contact details were available.

Where possible, we calculated missing values (such as SDs) from the available data (P values, t values, CIs or standard errors) (Higgins 2011).

If insufficient data were available to calculate missing values, we only analysed the available data. We narratively described results from studies with missing data. We addressed the issue of the missing data and their potential impact on the findings of the study in the Discussion.

Assessment of heterogeneity

The target population of this review, patients with oral poisoning, is inherently heterogeneous with respect to the type, dose and timing of poison intake. However, the target audience for delivering this intervention, laypeople, are likely not capable of

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differentiating between these differences. Therefore, a certain degree of heterogeneity in the results is unavoidable.

Our analyses are stratified based on type of intervention. We assessed heterogeneity by inspection of the forest plot and by using the Chi²-test and the I² statistic. We considered the Chi² statistic to be significant at P < 0.10. For interpretation of the I², we followed the guidance of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

When I² was at least 80% and the P value of the Chi² test was less than 0.1, we considered heterogeneity to be substantial, whereas for I² values below 40%, we considered heterogeneity to be unimportant. When heterogeneity was substantial, we examined the direction of the effects before making a decision whether to report the pooled result or describe the effects narratively.

Assessment of reporting biases

We planned methods for assessing reporting biases, but we could not perform them (New Reference). See Differences between protocol and review section.

Data synthesis

Where possible, we performed meta-analyses. We pooled data if there were two or more studies on the same intervention that assessed the same outcome and provided sufficient data. We did not combine outcomes with different timings into a single meta-analysis. We analysed different comparisons as separate analyses. We performed meta-analyses using a random-effects model, given the anticipated variation between studies. For dichotomous outcomes, we used the Mantel-Haenszel method, while for continuous outcomes, we used the inverse variance method. In case of dichotomous outcomes with no or few events in one of the test groups, we used the Peto OR method, if criteria were met according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Given the large number of interventions in this review, we considered the possibility of a network meta-analysis (NMA). However, due to the paucity of data and the heterogeneity in reported outcomes, this was not an option. In future updates of this review, we will consider this possibility again if there are sufficient data.

Subgroup analysis and investigation of heterogeneity

To investigate potential heterogeneity, we could have theoretically performed four possible subgroup analyses.

- Different drugs taken. We hypothesized that for the intervention activated charcoal, drugs with a higher or a lower affinity for activated charcoal would be taken up to a lesser or higher extent in the body, while for cathartics, drugs that are absorbed faster would be less effectively flushed out of the body than drugs with a slower absorption rate.
- Time point of the intervention. We hypothesized that the later an intervention is performed, the less efficacious it is in lowering the uptake of the drug.
- Co-interventions administered. We hypothesized that differing co-interventions, such as the administration of a hospital treatment (e.g. gastric lavage), could influence the efficacy of the intervention investigated.
- Type of adverse event experienced. We hypothesized that for the combined outcome 'occurrence of adverse events', different

types of adverse events might be experienced to a different degree for a certain intervention.

Of these potential analyses, we could perform only the latter two because of the paucity of data.

Sensitivity analysis

We had planned to perform a sensitivity analysis by excluding studies at high or unclear risk of bias for sequence generation, allocation concealment, incomplete outcome reporting or other sources of bias, and then comparing the results with the initial analysis. However, we were not able to combine sufficient studies into a meta-analysis for this analysis based on risk of bias of the individual studies.

We had also planned to perform sensitivity analyses in case we were required to impute data for some studies to enable meta-analysis. We would have excluded the studies with imputed data and compared the results to the initial analysis. However, we were not able to impute data.

See Differences between protocol and review section.

'Summary of findings' table

We assessed the certainty of the body of evidence from the included studies according to the methodology described by the GRADE working group (Atkins 2004). The GRADE approach assesses the certainty of evidence for separate outcomes across the different studies in five domains: limitations in study design, consistency, imprecision, indirectness and publication bias. RCTs start with a level of high-certainty evidence, which can be downgraded by one (serious limitations) or two (very serious limitations) levels for each of these domains. The certainty of evidence can therefore be high, moderate, low or very low. For the assessment of the GRADE domain 'limitations in study design', we decided to downgrade the certainty of evidence for an outcome if we judged one of the studies contributing to this outcome to be at high risk of bias in one of following domains: selection bias, detection bias, attrition bias or other bias. We decided not to take into account domains with unclear risk of bias to make this judgment. For the assessment of the GRADE domain 'imprecision' according to the guidance of the GRADE working group (Guyatt 2011), we decided to downgrade the certainty of evidence for an outcome:

- if the optimal information size criterion was not met and total sample size of studies contributing to the outcome was low (fewer than 400 participants) for continuous outcomes or there was a low number of events (fewer than 300 events) for dichotomous outcomes;
- if the CIs were wide (including both the line of no effect and an appreciable benefit or harm, i.e. a 25% increase or decrease in risk for dichotomous outcomes or a 50% increase or decrease in mean difference for continuous outcomes); or
- if there was a lack of data to judge the prior two criteria.

We created a 'Summary of findings' table, using the online GRADEpro Guideline Development Tool (GRADEpro GDT 2015), for the most relevant comparison of interventions in a first aid setting: single-dose activated charcoal (SDAC) versus no intervention. We created additional 'Summary of findings' tables for the other most clinically relevant comparisons involving single- and multi-dose activated charcoal: SDAC plus hospital intervention versus

hospital intervention alone, MDAC plus hospital intervention versus SDAC plus hospital intervention, MDAC plus hospital intervention versus hospital intervention alone, and syrup of ipecac versus no intervention. We also created 'Summary of findings' tables for the other identified comparisons, but we placed these in the Appendices.

We have included all primary and secondary outcomes of this review in our 'Summary of findings' tables. For outcomes such as severity of symptoms, studies reported multiple outcomes (e.g. incidence of clinical improvement, incidence of intubation requirement, incidence of convulsions etc.). As 'Summary of findings' tables should include no more than seven outcomes, we chose the clinically most relevant outcomes together with a clinical expert (PD).

Figure 1. Study selection flow diagram.

R E S U L T S

Description of studies

Results of the search

Our search strategies identified a total of 11,582 references. After removing 1859 duplicates and screening titles and abstracts, we assessed 78 full-text records for eligibility. At this stage we included 20 studies, reported in 27 records, and we then included an additional four studies after screening reference lists of included studies and systematic reviews retrieved with the database searches and similar articles in PubMed. Figure 1 shows the flowchart of the study selection.

Included studies

We included 24 studies reported in 31 publications and involving a total of 7099 participants randomized to different treatment groups. Only one study took place in a pre-hospital setting (Wax 1999), whereas the rest were in hospitals.

Nineteen studies assessed the effects of single-dose activated charcoal (SDAC), either administered alone (Amigó Tadín 2002; Merigian 1990; Underhill 1990), in adjuvant to hospital treatment (Behnoush 2009; Brahmi 2006; Comstock 1982; Cooper 2005; Crome 1983; De Silva 2003; Eddleston 2008; Hultén 1988; Merigian 2002; Roberts 2006), combined with a cathartic (James 1995; Passeron 1989), or combined with syrup of ipecac (Albertson 1989; Kornberg 1991; Kulig 1985; Pond 1995).

Seven studies looked at the effect of multi-dose activated charcoal (MDAC) either in adjuvant to hospital treatment (Behnoush 2009; Bouget 1989; Brahmi 2006; De Silva 2003; Eddleston 2008; Roberts 2006), or combined with cathartics and in adjuvant to hospital treatment (Montoya-Cabrera 1999).

Six studies investigated syrup of ipecac alone (Amigó Tadín 2002; Wax 1999), or followed by SDAC and a cathartic (Albertson 1989; Kornberg 1991; Kulig 1985; Pond 1995).

Table 2 contains an overview of the comparisons made in the different studies.

Excluded studies

We excluded 47 studies after full-text evaluation (Characteristics of excluded studies). We excluded 11 studies because of an ineligible study population (not oral poisoning patients or patients with chronic poisoning), 30 studies because of an intervention that did not meet our selection criteria and 5 because of an inappropriate comparison. Furthermore, we excluded one recent study, published as an abstract only (Escalante 2016), because of a lack of prospective trial registration, in accordance to the editorial policies of the Cochrane Injuries review group.

Risk of bias in included studies

We did not judge any study to be at low risk of bias on all domains investigated. We scored two studies as having a low risk of bias for all but one domain: in one study there was a risk of selective reporting (De Silva 2003), and in the other there was a risk of performance bias (Eddleston 2008). All other studies were at high or unclear risk of bias for two or more domains. Six studies were at high risk of bias in at least four domains (Albertson 1989; Crome 1983; Kornberg 1991; Merigian 2002; Pond 1995; Wax 1999), whereas 12 studies were at unclear risk of bias in three or more domains (Amigó Tadín 2002; Behnoush 2009; Bouget 1989; Brahmi 2006; Comstock 1982; Crome 1983; Hultén 1988; Ilett 1977; Montoya-Cabrera 1999; Passeron 1989; Sue 1994; Underhill 1990). Figure 2 and Figure 3 provide an overview of the risk of bias across domains and studies, and detailed judgments by domain can be found for each included study in the Characteristics of included studies table.

Figure 2.

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Figure 2. (Continued)

Figure 3.

Allocation

In general, randomization and allocation concealment was inadequately performed or poorly reported. The population was sufficiently randomized and adequately reported in six studies only (Bouget 1989; De Silva 2003; Eddleston 2008; Hultén 1988; Ilett 1977; Roberts 2006). In four studies the allocation concealment was adequate (Cooper 2005; De Silva 2003; Eddleston 2008; Roberts 2006).

Blinding

Most studies either did not blind or did not report on blinding of the participants and personnel. This is likely due to the nature of the interventions, which makes it difficult to perform adequate blinding. However, this might lead to performance bias, for example, because of differential administration of co-interventions. One study that combined activated charcoal with different cathartics reported blinding both participants and personnel (James 1995), while another study testing multiple versus single doses of activated charcoal blinded the treating physicians by making sure research assistants cleaned the participants and their bedclothes after each activated charcoal treatment (De Silva 2003). Blinding of outcome assessors was not common, but seven studies did take this step (Comstock 1982; De Silva 2003; Eddleston 2008; James 1995; Montoya-Cabrera 1999; Roberts 2006; Underhill 1990).

Incomplete outcome data

Only three studies were at high risk of attrition bias (Comstock 1982; Crome 1983; Passeron 1989), and three were at unclear risk (Amigó Tadín 2002; Behnoush 2009; Bouget 1989). All other studies showed no evidence of incomplete outcome data.

Selective reporting

Overall there was a high risk of reporting bias. Only a third of the studies were at low risk (Amigó Tadín 2002; Cooper 2005; Eddleston 2008; Hultén 1988; Kornberg 1991; Merigian 1990; Roberts 2006; Wax 1999).

Other potential sources of bias

Fifteen studies were at low risk of other potential sources of bias, and we assessed nine studies as being at high risk of bias for reasons other than those mentioned above.

In Albertson 1989, actual poisoning was not verified for 25% of the participants by means other than history. Furthermore, in Wax 1999, there was no confirmation of actual ingestion or uptake of the drug.

In another study, investigators suspected a clinical difference between the groups receiving the MDAC intervention versus the SDAC control, based on divergent carbamazepine kinetics during

the initial six hours of the treatment period, when both groups had received only one dose of activated charcoal (Brahmi 2006). Also in Montoya-Cabrera 1999, the hepatic toxicity marker values suggest there might be a clinically meaningful difference between the two treatment groups. This could create a bias in effectiveness of the treatment, because of differences in degree and type of poisoning.

In Comstock 1982 there was a potential bias in the selection of the study population since participants were selected at the discretion of the attending physician.

Crome 1983 did not find significant amounts of any drugs in 11 of the 48 participants, and 7 of them had not taken any tricyclic antidepressant (although this was a criterion for inclusion). Furthermore, the role of the study funder was not clear.

Two studies included only asymptomatic participants, who are less likely to experience a benefit from any treatment (Merigian 1990; Wax 1999).

Merigian 2002 performed only post hoc analyses according to clinical severity, and there was no follow-up after discharge from the hospital.

In Roberts 2006 it is not entirely clear, even to the authors, what exactly is measured with the digoxin assay used in the study. The fact that both active cardenolides and metabolites might be detected by the assay compromise the results of these analyses, potentially explaining the wide variability observed. Furthermore, only participants with mild intoxication were included in this analysis, as the severe cases were treated with Fab antitoxin or transferred to a tertiary hospital, but these patients might have shown the biggest effect (Roberts 2006).

In Wax 1999, the authors reported dichotomous outcomes but performed measurement using an ordinal scale.

Effects of interventions

See: **Summary of findings for the main comparison** SDAC versus no intervention for first aid in patients with acute oral poisoning; **Summary of findings 2** SDAC + hospital intervention versus hospital intervention alone for first aid in patients with acute oral poisoning; **Summary of findings 3** MDAC + hospital intervention versus SDAC + hospital intervention for first aid in patients with acute oral poisoning; **Summary of findings 4** SDAC versus syrup of ipecac for first aid in patients with acute oral poisoning; **Summary of findings 5** MDAC + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning; **Summary of findings 6** Syrup of ipecac versus no intervention for first aid in patients with acute oral poisoning

See Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5; Summary of findings 6; Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7.

A. First aid interventions that limit or delay the absorption of the poison in the body

1. Single-dose activated charcoal versus no intervention

Two studies compared a single dose of activated charcoal versus no intervention (Merigian 1990; Underhill 1990). Underhill 1990 included 25 participants presenting in the emergency

department with acute paracetamol overdose. Recruitment in the control group was stopped early for ethical reasons, as blood levels of paracetamol kept rising over time. Merigian 1990 included 820 participants presenting at the emergency department with self-reported oral overdose in general. This study subdivided participants into a symptomatic and an asymptomatic group, for which treatments differed. Only the 451 asymptomatic participants, who received either a single dose of activated charcoal or were kept for observation, were within scope of this review. For a detailed summary of the outcomes, we refer to the Data and analyses section. Below we provide a narrative overview. See Summary of findings for the main comparison.

Primary outcomes

Incidence of mortality

The identified studies either did not collect or did not report outcomes related to mortality.

Adverse events

The only adverse event Underhill 1990 reported in response to SDAC was vomiting, which occurred in 4/20 participants compared to 0/5 in the control group (Peto OR 4.17, 95% CI 0.30 to 57.26; Analysis 1.1). Merigian 1990 reported no adverse events in any treatment group (451 participants). We assessed this evidence as being of very low certainty because of limitations in study design, imprecision due to a low event number and indirectness.

Incidence and severity of poisoning symptoms

Only Merigian 1990 reported an outcome related to symptom severity. In 451 asymptomatic participants presenting to the emergency department, no participants experienced events of clinical deterioration in either group (Table 3). We assessed this evidence as being of very low certainty because of limitations in study design, imprecision due to a low event number and indirectness.

Secondary outcomes

Duration of symptoms

The identified studies either did not collect or did not report outcomes related to symptom duration.

Drug absorption

Underhill 1990 measured drug levels of paracetamol before treatment and at several time points after treatment. However, the study reported none of the pre-defined outcomes of interest in our protocol, nor could we derive them from the data provided; therefore we could make no reliable estimation of drug absorption from the available data.

Incidence of hospitalization

The identified studies either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

Merigian 1990 reported the number of participants admitted to the ICU department, which was 1/220 in the intervention group and 0/231 participants in the control group (Peto OR 7.77; 95% CI 0.15 to 391.93; Table 3). We assessed this evidence as being of very low

certainty, downgraded for limitations in study design, imprecision due to a low number of events and indirectness.

Summary for this comparison

We were uncertain about the effect of SDAC compared to no intervention on the incidence of ICU admission or the incidence of clinical deterioration (very low certainty due to limitations in study design, imprecision and indirectness). One study described a single type of adverse event in response to the treatment, vomiting, but we are uncertain about the effect (very low-certainty evidence due to limitations in study design, imprecision and indirectness).

2. Single-dose activated charcoal plus hospital intervention versus hospital intervention alone

Seven trials used single-dose activated charcoal (SDAC) in adjuvant to established hospital treatments (Comstock 1982; Cooper 2005; Crome 1983; Eddleston 2008; Hultén 1988; Merigian 2002; Roberts 2006). These hospital treatments consisted of supportive treatments to maintain vital parameters plus poison-specific treatments, but in most studies this also included gastric lavage (Comstock 1982; Crome 1983; Eddleston 2008; Hultén 1988; Roberts 2006). Crome 1983 and Hultén 1988 specifically included participants with tricyclic antidepressant overdose, while the other studies did not define a specific toxic syndrome. Roberts 2006 investigated drug uptake in a subpopulation of participants entering the Eddleston 2008 study, with yellow oleander seed poisoning. For a detailed summary of the outcomes, we refer to the Data and analyses section. Below we provide a narrative overview. See Summary of findings 2.

Primary outcomes

Incidence of mortality

Two studies reported the impact of SDAC on mortality (Cooper 2005; Eddleston 2008). Both studies included participants with a variety of toxic syndromes, so we considered it appropriate to pool these results. Moreover, from a layperson's perspective, it is usually impossible to distinguish different toxic syndromes, let alone decide on the appropriateness of administering SDAC in case of a specific syndrome. The statistical results were mainly determined by the large study, Eddleston 2008 (Peto OR 1.04, 95% CI 0.79 to 1.37; 3425 participants; 2 studies; Analysis 2.1). We did not identify important heterogeneity (P = 0.30, I^2 = 7%). Evidence was of low certainty, downgraded for imprecision due to wide confidence intervals and indirectness.

Adverse events

Three studies reported on adverse events in relation to administering SDAC (Cooper 2005; Eddleston 2008; Merigian 2002). Two studies reported the occurrence of vomiting (Cooper 2005; Merigian 2002), while Eddleston 2008 reported the absence of bowel sounds as a proxy for constipation. We considered a combined estimate of adverse events to be appropriate, given the wide variety in toxic syndromes included in the different studies and the inability of laypeople to distinguish between different toxic syndromes. However, this resulted in considerable heterogeneity (P = 0.002, I^2 = 83%) with different directions of effect. We performed a subgroup analysis by reported symptom, showing between-group differences (P = 0.02, I^2 = 83%), which decreased but did not fully eliminate the heterogeneity. The risk ratio for the outcome occurrence of vomiting was 1.44 (95% CI 0.88 to 2.37; 1806

participants; 2 studies) and still showed substantial unexplained heterogeneity (P = 0.08, I^2 = 68%). The RR for the sub-outcome, absence of bowel sounds, was 0.41 (95% CI 0.17 to 1.00; 3098 participants; 1 study; Analysis 2.2). The evidence on adverse events was of very low certainty because of inconsistency between studies, imprecision (low number of events) and indirectness.

Incidence and severity of symptoms of poisoning

One study evaluated the incidence of clinical deterioration, which was absent in both an intervention group of 455 participants and a control group of 1075 participants (Merigian 2002; Table 3). This evidence was of very low certainty, downgraded due to limitations in study design, imprecision (low number of events) and indirectness.

Crome 1983 and Hultén 1988 expressed the grade of coma using the Matthew-Lawson coma scale at 4 h, 8 h and 24 h after hospital admission. The median coma score scales of intervention and control groups were similar in the study of 16 participants (Crome 1983; Table 3). The proportion of participants with a coma scale of III or IV were also similar in Hultén 1988, with 77 participants (Table 3). Evidence was of very low certainty, downgraded for limitations in study design, imprecision due to a low number of events and a low sample size and indirectness.

Eddleston 2008 reported the incidence of participants with yellow oleander seed poisoning, who needed specialized treatment, namely cardiac pacing or Fab antitoxin treatment (Eddleston 2008). The risk ratio was 1.01 (95% CI 0.79 to 1.30, P = 0.93, 1104 participants; Table 3). This evidence was of low certainty, downgraded for imprecision due to a low number of events and indirectness.

Four studies reported on the need for intubation and/or ventilation (Cooper 2005; Eddleston 2008; Hultén 1988; Merigian 2002). In Merigian 2002 these data were only available for participants admitted to the ICU. We considered it appropriate to combine the results, given the multiple or unspecified toxic syndromes included in three out of four individual studies, and the inability of laypeople to distinguish between ingested toxins. The combined result showed substantial heterogeneity and different directions of effect, so we do not present it (P = 0.04; I^2 = 63%; Analysis 2.3). A possible reason for the observed heterogeneity may have been the co-interventions, i.e. whether participants received gastric lavage as part of the hospital treatments. A subgroup analysis suggested there may be between-group differences between participants who received gastric lavage prior to receiving SDAC and those who did not (P = 0.005, I^2 = 87.6%). The summary estimate in the subgroup with gastric lavage was RR 0.95 (95% CI 0.70 to 1.27, 3175 participants, 2 studies, P = 0.71). In the subgroup without gastric lavage the RR was 2.61 (95% CI 1.38 to 4.93, 387 participants, 2 studies, P = 0.003), in favour of not receiving SDAC. In addition, Hultén 1988 made a subcomparison of the need for ventilation with a respirator (RR 0.28, 95% CI 0.06 to 1.22, 77 participants, P = 0.09; Table 3). Evidence on ventilation was of low certainty, downgraded for imprecision (low number of events and wide confidence intervals) and indirectness.

Two studies, Eddleston 2008 and Hultén 1988, studied the incidence of convulsions. We considered combining these outcomes appropriate, given the inability of laypeople to make a distinction between different toxic syndromes. A combined

estimate of these studies, however, had substantial heterogeneity (P = 0.03; I^2 = 79%) and a different direction of effect, so we only report the individual study results. The individual estimates were RR 1.87 (95% CI 0.75 to 4.67, 3098 participants; Eddleston 2008) and RR 0.28 (95% CI 0.06 to 1.22, 77 participants; Hultén 1988; Analysis 2.4). Exploring heterogeneity in a meta-analysis with only two studies is difficult, so explanations for the observed differences between studies remain speculative. Possible reasons might be the small study sample in Hultén 1988. Alternatively, true differences in patient population might explain the differences, as Hultén 1988 specifically recruited participants with tricyclic antidepressant poisoning, while most participants in Eddleston 2008 took an overdose of pesticides or yellow oleander seeds. This evidence was of very low certainty, downgraded for inconsistency between studies, imprecision (wide confidence intervals and low number of events) and indirectness.

Hultén 1988 recorded some additional clinical parameters in their 77 participants, as measures of poisoning severity: systolic blood pressure, heart rate and incidence of cardiac arrhythmias, at 4 h, 8 h and 24 h after treatment (Table 3). These numbers were not shown to differ between treatments. The certainty of evidence for these parameters was rated as very low, due to limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Secondary outcomes

Duration of symptoms

Three studies measured length of intubation (Eddleston 2008; Hultén 1988; Merigian 2002). Combination of the studies' results in a meta-analysis was not feasible, due to differences in reporting. Eddleston 2008 reported medians with interquartile ranges, and there was no demonstrable difference. Authors did not report the number of participants in this analysis. Merigian 2002 reported length of intubation as means without a measure of spread or the number of participants in the analysis, and likewise, authors could not show a difference between intervention and control (Analysis 2.5). Hultén 1988 reported the proportion of participants that were intubated for longer than 8 h, which was similar between intervention and control (RR 0.56, 95% CI 0.19 to 1.67, 77 participants, P = 0.30; Hultén 1988; Table 3). This evidence was rated to be of low certainty, downgraded for imprecision due to a low number of events or lack of data, plus indirectness.

Drug absorption

Three included studies measured drug absorption (Comstock 1982; Hultén 1988; Roberts 2006). Comstock 1982, with 339 participants, only reported increases in blood drug concentrations over time, without reporting any of our pre-specified outcomes of interest. Hultén 1988 presented the course of tricyclic antidepressant levels in the blood of 77 participants graphically, and reported narratively that there was no demonstrable difference in AUC, C_{max} or $T_{1/2}$ between treatments (Hultén 1988). Therefore, the only numeric data available were on the AUC, C_{max} and T_{max} of cardenolides from yellow oleander seeds, measured by Roberts 2006 in a subset of 68 participants from the Eddleston study. Authors reported results as median with interquartile ranges (IQR) and could not show a difference between treatments (Analysis 2.6; Analysis 2.7; Analysis 2.8). The evidence on the pharmacokinetic parameters was of very low certainty, due to limitations in study design, imprecision (low sample size) and indirectness.

Incidence of hospitalization

Merigian 2002 reported the incidence of hospitalization. The results favoured no treatment over SDAC (RR 1.57, 95% CI 1.22 to 2.02, 1479 participants, P < 0.001; Analysis 2.9). We assessed this evidence as being of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Incidence of ICU admission

Merigian 2002 reported the incidence of ICU admission in favour of no treatment with SDAC (RR 2.33, 95% CI 1.42 to 3.82, 1479 participants, P < 0.001; Analysis 2.10). This evidence was of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Summary for this comparison

SDAC as adjuvant to supportive hospital treatments may have little or no influence on one of our primary outcomes, incidence of mortality, while we are uncertain about its effect on another primary outcome, adverse events due to the intervention. In addition, SDAC plus hospital treatments may have little or no influence on the primary outcomes of need for intubation, need for cardiac pacing or antitoxin treatment in cases of yellow oleander poisoning, or the secondary outcome, length of intubation. We are uncertain about the effect of SDAC in addition to hospital treatments on the incidence of clinical deterioration, Matthew-Lawson coma scale scores, incidence of convulsions, blood pressure, heart rate, cardiac arrhythmias, and the secondary outcomes of drug absorption and incidence of hospital or ICU admission. The evidence collected is of low to very low certainty, due to limitations in study design, indirectness and/or imprecision.

3. Multi-dose activated charcoal plus hospital intervention versus single-dose activated charcoal plus hospital intervention

Five trials compared single-dose (SDAC) versus multi-dose activated charcoal (MDAC), in adjuvant to hospital treatments (Behnoush 2009; Brahmi 2006; De Silva 2003; Eddleston 2008; Roberts 2006). The identified trials studied the following toxic overdoses: carbamazepine (Behnoush 2009; Brahmi 2006), yellow oleander (De Silva 2003; Roberts 2006), and a combination of toxic syndromes (Eddleston 2008). In all studies except for Brahmi 2006, supportive treatments included gastric lavage. Behnoush 2009 did not report any outcomes of interest for this review. See Summary of findings 3.

Primary outcomes

Incidence of mortality

Incidence of mortality was an outcome of interest in De Silva 2003 and Eddleston 2008. We considered it appropriate to combine the findings given the similar populations studied. Nevertheless, the meta-analysis resulted in an estimate with substantial heterogeneity (P = 0.04, I^2 = 76%), albeit the same direction of effect. The pooled risk ratio was 0.59 (95% CI 0.21 to 1.63; 3476 participants; 2 studies; Analysis 4.1). Reasons for the observed heterogeneity were not immediately clear, as both the provided interventions and the population studied are remarkably similar. Eddleston 2008 included a broader range of toxic syndromes; however, including only the subpopulation of participants with yellow oleander poisoning (SDAC: 26/549 and MDAC: 23/541) would not change the conclusions made (P = 0.06, I^2 = 71%). There are some factors that might explain the differences

observed, such as a longer treatment in De Silva 2003 (activated charcoal up to 72 h) compared to Eddleston 2008 (activated charcoal up to 24 h) or differences in the compliance rate with the treatment (reported to drop to 66% by the final dose by Eddleston 2008 but claimed to be ensured in all cases by De Silva 2003). However, these explanations remain speculative, and if there are more studies in a future update, we may be able to show more robust evidence and clarify the heterogeneity issue. We considered the evidence here to be of very low certainty, due to inconsistency between studies, imprecision (wide confidence intervals) and indirectness.

Adverse events

Two studies reported the incidence of adverse events in response to the intervention (De Silva 2003; Eddleston 2008). We considered combining the results of these studies appropriate, given the similar study population. The combined result (Peto OR 3.55, 95% CI 1.85 to 6.79; 3476 participants; 2 studies) contained a substantial degree of heterogeneity (P = 0.08, I² = 66.8%), but with the same direction of effect. Reasons for this heterogeneity remain speculative, but it could be due to differing definitions and diagnostic methods for adverse events, for example absent bowel sounds in Eddleston 2008 (Peto OR 2.34, 95% CI 1.05 to 5.21; 3075 participants, P = 0.04) versus abdominal discomfort/diarrhoea in De Silva 2003 (Peto OR 7.82, 95% CI 2.59 to 23.58; 401 participants, P < 0.001; Analysis 4.2). Both studies suggest that the number of adverse events may increase in case of MDAC, compared to SDAC. This evidence was of low certainty, downgraded for imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence and severity of symptoms of poisoning

Both De Silva 2003 and Eddleston 2008 reported on the need for cardiac pacing or administration of a Fab antitoxin, treatments used in severe cases of yellow oleander poisoning. We considered it appropriate to combine results, given the similar patient populations studied. The combined effect estimate (RR 0.26, 95% CI 0.02 to 4.18; 1490 participants; 2 studies) resulted in considerable heterogeneity (P = 0.005, I² = 87%; Analysis 4.3). As for mortality, the reasons for the observed heterogeneity are not immediately clear and remain speculative. We considered evidence to be of very low certainty, due to imprecision (low numbers of events and wide confidence intervals), inconsistency between studies and indirectness.

De Silva 2003 also recorded the incidence of life-threatening arrhythmias after 24 h, which may be lower for the group receiving SDAC (RR 0.21, 95% CI 0.06 to 0.71, 385 participants, P = 0.01; Analysis 4.4). Evidence was of low certainty, downgraded for imprecision due to a low number of events and indirectness.

Another outcome De Silva 2003 reported in their study with 401 participants was the need for atropine, expressed as both the amount of atropine administered and the number of boluses administered. Both the amount (mg) of atropine administered (MD −1.60, 95% CI −2.25 to −0.95, P < 0.001; Analysis 4.5) and the median number of boluses (Analysis 4.6) were higher in the group receiving SDAC. We assessed the evidence as being of moderate certainty, downgraded for indirectness.

Two studies reported the need for intubation (Brahmi 2006; Eddleston 2008). We decided to combine these results, as from the point of view of laypeople, the focus of this review, it is usually impossible to distinguish between toxic syndromes or adapt the provided intervention accordingly. There may be little or no effect on the need for intubation (RR 1.01, 95% CI 0.75 to 1.38, 3097 participants, P = 0.93; Analysis 4.7). There was no heterogeneity between studies (P = 0.98, I² = 0%). The evidence was of low certainty, downgraded due to imprecision (low number of events and wide confidence intervals) and indirectness.

Finally, Eddleston 2008 reported the incidence of convulsions (RR 1.09, 95% CI 0.52 to 2.32, 3085 participants, P = 0.82; Analysis 4.8). Evidence was of low certainty, downgraded due to imprecision (low number of events and wide confidence intervals) and indirectness.

Secondary outcomes

Duration of symptoms

One study in six participants reported the duration of coma as a measure of symptom duration (Brahmi 2006). The mean difference was −9.00 h (95% CI −14.79 to −3.21, P = 0.002), in favour of MDAC (Analysis 4.9). We considered this to be evidence of very low certainty, downgraded for limitations in study design, imprecision (small sample size) and indirectness.

Brahmi 2006 and Eddleston 2008 also reported duration of intubation. Due to differences in reporting, it was not possible to combine the estimates. The mean difference reported by Brahmi 2006 is −12.30 h (95% CI −18.56 to −6.04, 6 participants, P < 0.001). Eddleston 2008 reported medians with IQR; however, authors made no statement of effectiveness. The number of participants in the analysis was not clear either (Analysis 4.10). This evidence was of very low certainty, downgraded for inconsistency between studies, imprecision (low sample size and lack of data) and indirectness.

Drug absorption

Two studies, Brahmi 2006 and Roberts 2006, reported on pharmacokinetic parameters as measures of drug absorption. Differences in reporting precluded meta-analysis.

Both studies reported the C_{max}. The mean difference reported by Brahmi 2006 was 0.40 mg/L (95% CI −4.89 to 5.69, 6 participants, P = 0.88). Roberts 2006 reported C_{max}, as medians with IQR, demonstrating no difference between intervention and control (participants = 64, P > 0.05; Analysis 4.11). AUC and T_{max} were similar between treatments (64 participants, P > 0.05; Analysis 4.12; Analysis 4.14). In addition, Brahmi 2006 measured the $T_{1/2}$ which was in favour of MDAC (MD −15.32 h (95% CI −21.84 to −8.80, 6 participants, P < 0.001; Analysis 4.13). The evidence was of very low certainty, downgraded for limitations in study design, imprecision (low sample size) and indirectness.

Incidence of hospitalization

The identified studies either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

De Silva 2003 reported the incidence of ICU admissions. The risk ratio suggests MDAC may have a strong effect on reducing ICU admissions (RR 0.31, 95% CI 0.12 to 0.83, 401 participants, P = 0.02; Analysis 4.15). The presented evidence was of low certainty, downgraded for imprecision (low number of events) and indirectness.

First aid interventions by laypeople for acute oral poisoning (Review)

Summary for this comparison

The evidence that we have collected concerning the use of single- versus multi-dose activated charcoal in adjuvant to hospital treatments is of moderate to very low certainty. There may be little or no difference in the incidence of convulsions and the need for intubation between MDAC plus hospital treatments and SDAC plus hospital treatments. On the other hand, there may be a favourable effect for MDAC on the incidence of life-threatening cardiac arrhythmias and ICU admissions, while it probably decreases the number of atropine boluses and total amount of atropine administered. Low-certainty evidence suggests, however, that MDAC may come with an increased risk of adverse events. We are uncertain about the effects of MDAC plus hospital treatments on mortality, the need for cardiac pacing or antitoxin treatment, symptom duration and drug absorption.

4. Single-dose activated charcoal versus syrup of ipecac

One study with 34 participants compared SDAC versus syrup of ipecac in oral poisoning participants with mild levels of intoxication (defined as a Glasgow Coma Scale score of more than 12; Amigó Tadín 2002). The study specifically included participants presenting with oral overdoses of anti-inflammatory, psychotropic or analgesic drugs. Participants received no additional treatments. See Summary of findings 4.

Primary outcomes

Incidence of mortality

The identified study did not collect outcomes related to mortality.

Adverse events

Amigó Tadín 2002 reported the incidence of adverse events encountered (RR 1.24, 95% CI 0.26 to 5.83, 34 participants, P = 0.79; Analysis 3.1). Evidence was of very low certainty, downgraded for limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence and severity of symptoms of poisoning

The identified study measured participants' poisoning symptoms 1 h after treatment (Amigó Tadín 2002). The mean difference in Glasgow Coma Scale scores between treatments was −0.15 (95% CI −0.43 to 0.13, 34 participants, P = 0.29; Analysis 3.2). Furthermore, the study reported mean arterial blood pressure (MD 7.00 mmHg, 95% CI −3.56 to 17.56, 34 participants, P = 0.19; Analysis 3.3), heart rate (MD −2.39 bpm, 95% CI −15.58 to 10.80, 34 participants, P = 0.72; Analysis 3.4) and respiratory rate (MD 1.12 breaths/min, 95% CI −1.69 to 3.93, 34 participants, P = 0.44; Analysis 3.5) as measures of intoxication. The collected evidence was of very low certainty, downgraded for limitations in study design, imprecision (low sample size) and indirectness.

Secondary outcomes

Duration of symptoms

The identified study did not collect outcomes related to symptom duration.

Drug absorption

The identified study did not collect outcomes related to drug absorption.

Incidence of hospitalization

The identified study did not collect outcomes related to incidence of hospitalization.

Indicence of ICU admission

The identified study did not collect outcomes related to incidence of ICU admission.

Summary for this comparison

We identified evidence of very low certainty, originating from one study (Amigó Tadín 2002). We are uncertain about any difference between SDAC and syrup of ipecac concerning poisoning symptoms or incidence of adverse events.

5. Multi-dose activated charcoal plus hospital treatment versus hospital treatment alone

We found three studies comparing the administration of MDAC in adjuvant to hospital treatments versus hospital treatments alone (Bouget 1989; Eddleston 2008; Roberts 2006). For most participants in Eddleston 2008, who had a variety of intoxications, hospital treatments included gastric lavage. Roberts 2006 studied a subgroup of participants from the Eddleston study, those with yellow oleander seed poisoning. Bouget 1989 included 36 participants with benzodiazepine poisoning, but no numeric outcomes were reported in this study. See Summary of findings 5.

Primary outcomes

Incidence of mortality

Eddleston 2008 reported the incidence of mortality, which may not differ between intervention and control (RR 0.94, 95% CI 0.72 to 1.22, 3085 participants, P = 0.64; Analysis 5.1). The evidence was of low certainty, downgraded for imprecision (low number of events and wide confidence intervals) and indirectness.

Adverse events

Eddleston 2008 reported one adverse event, incidence of absent bowel sounds (RR 1.02, 95% CI 0.52 to 1.98, 3085 participants, P = 0.97; Analysis 5.2). Evidence was of low certainty, downgraded for imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence and severity of symptoms of poisoning

Eddleston 2008 reported several markers of intoxication, including the need for intubation (RR 0.97, 95% CI 0.71 to 1.33, 3085 participants, P = 0.87; Analysis 5.3), seizures (RR 2.03, 95% CI 0.82 to 5.02, 3085 participants, P = 0.12; Analysis 5.4) and need for cardiac pacing/Fab antitoxin treatment in participants with yellow oleander poisoning (RR 0.86, 95% CI 0.66 to 1.13, 1095 participants, P = 0.28; Analysis 5.5). Evidence was of low certainty, downgraded for imprecision (low number of events and wide confidence intervals) and indirectness.

Secondary outcomes

Duration of symptoms

Eddleston 2008 reported length of intubation as a measure of symptom duration. It was expressed as a median plus IQR, and it may not be different between groups (Analysis 5.6). The evidence was of low certainty, downgraded for imprecision (lack of data) and indirectness.

Drug absorption

Roberts 2006 analysed cardenolide pharmacokinetic parameters in a subgroup of 76 participants from the Eddleston study, with yellow oleander poisoning. AUC, C_{max} and T_{max} were reported as medians with IQR, and there was no demonstrable difference between treatment groups (Analysis 5.7; Analysis 5.8; Analysis 5.9). Evidence was of very low certainty due to limitations in study design, imprecision (low sample size) and indirectness.

Incidence of hospitalization

The identified studies either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

The identified studies either did not collect or did not report outcomes related to incidence of ICU admission.

Summary for this comparison

The identified evidence on the use of MDAC in addition to hospital treatment is of low to very low certainty and originates from two studies, one of which is a subgroup analysis of the larger study (Eddleston 2008; Roberts 2006). MDAC plus hospital treatments may not be better than hospital treatments alone for mortality, symptoms of intoxication (need for intubation, seizures, cardiac pacing or antitoxin treatment), duration of intubation or absence of bowel sounds as adverse events. We are uncertain about the effects of MDAC on pharmacokinetic parameters of cardenolides.

B. First aid interventions that evacuate the poison from the gastrointestinal tract

B1. Emetics

6. Syrup of ipecac versus no intervention

One study compared ipecac versus observation in 103 cases of paediatric, asymptomatic toxic berry ingestion (Wax 1999). This study took place in a pre-hospital setting and did not include any other treatments. See Summary of findings 6.

Primary outcomes

Incidence of mortality

The identified study did not collect outcomes related to incidence of mortality.

Adverse events

The identified study reported on the incidence of several adverse events separately. As it was likely that one patient could encounter multiple adverse events, it was not possible to combine these into a composite outcome. Therefore, we present the risk ratios for the individually described adverse events. Participants receiving ipecac may show an increased risk of diarrhoea (RR 4.08, 95% CI 1.66 to 10.04, 103 participants, P = 0.002; Analysis 6.1) and sedation (RR 5.10, 95% CI 1.17 to 22.13, 103 participants, P = 0.03; Analysis 6.3), while there may be little or no difference for abdominal pain (RR 1.02, 95% CI 0.07 to 15.87, 103 participants, P = 0.99; Analysis 6.2) or agitation (RR 1.53, 95% CI 0.27 to 8.77, 103 participants, P = 0.63; Analysis 6.4). The evidence was of low certainty, downgraded for limitations in study design and imprecision (low number of events and wide confidence intervals).

Incidence and severity of symptoms of poisoning

The identified study did not collect outcomes related to incidence and severity of poisoning symptoms.

Secondary outcomes

Duration of symptoms

The identified study did not collect outcomes related to duration of poisoning symptoms.

Drug absorption

The identified study did not collect outcomes related to drug absorption.

Incidence of hospitalization

One patient in the intervention group was referred to the emergency department, compared to none in the control group (Wax 1999). The Peto OR was 7.54 (95% CI 0.15 to 379.83, 103 participants, P = 0.31; Table 3). None of the 103 participants were hospitalized (Table 3). The evidence was of low certainty, downgraded for limitations in study design and imprecision due to a small sample size and wide confidence intervals.

Incidence of ICU admission

As none of the participants were hospitalized, none could have been admitted to the ICU.

Summary for this comparison

We identified one study that compared syrup of ipecac versus home observation (Wax 1999). Authors did not report any clinical outcomes, but there may be little or no difference in emergency department referrals. In contrast, the incidence of adverse events (diarrhoea and sedation) may be larger. Evidence is of low certainty (downgraded for limitations in study design and imprecision).

7. Syrup of ipecac plus single-dose activated charcoal plus cathartics versus single-dose activated charcoal plus cathartics

We identified four studies that compared SDAC plus a cathartic (sorbitol or magnesium sulphate), preceded or not preceded by syrup of ipecac in participants presenting to an emergency department (Albertson 1989; Kornberg 1991; Kulig 1985; Pond 1995). None of the studies selected participants on a specific toxic syndrome. Kornberg 1991 focused on children under 6 years old, while Albertson 1989 and Pond 1995 included adults (specified as more than 18 years old or more than 13 years old, respectively). Kulig 1985 did not specify a certain age range. See Appendix 2.

Primary outcomes

Incidence of mortality

Two of the included studies reported on incidence of mortality, but neither study noted any events in the 573 participants across treatment groups (Kornberg 1991; Kulig 1985; Analysis 7.1). We considered this evidence to be of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Adverse events

Two studies reported the incidence of adverse events (Albertson 1989; Pond 1995), while one study reported the number of activated charcoal that was vomited as an adverse event (Kornberg 1991). We

combined these outcomes, as all studies included a wide variety of toxic syndromes. The meta-analysis favoured not using ipecac (RR 2.59, 95% CI 1.37 to 4.91, 764 participants, 3 studies, P = 0.003). We found no important heterogeneity (P = 0.29, I² = 19%; Analysis 7.2). This was evidence of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Incidence and severity of symptoms of poisoning

Three studies reported on the incidence of participants with clinical improvement during their stay in the emergency department (Kornberg 1991; Kulig 1985; Pond 1995). We considered a meta-analysis appropriate, given the wide variety of toxic syndromes included in the individual studies. The combined risk ratio was 1.00 (95% CI 0.83 to 1.21, 989 participants, 3 studies, P = 0.98), without evidence of important heterogeneity (P = 0.21, I² = 36%; Analysis 7.3). The evidence was of low certainty, downgraded for limitations in study design and indirectness.

Two trials studied the incidence of clinical deterioration during the emergency department stay (Kulig 1985; Pond 1995); we combined these in a meta-analysis, given the wide variety of toxic syndromes included in the individual studies. The pooled RR was 0.88 (95% CI 0.46 to 1.69, 970 participants, 2 studies, P = 0.70), with no apparent heterogeneity (P = 0.38, I² = 0%; Analysis 7.4). We considered this to be evidence of very low certainty, downgraded for limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Secondary outcomes

Duration of symptoms

The identified studies either did not collect or did not not report outcomes related to duration of poisoning symptoms.

Drug absorption

The identified studies either did not collect or did not report outcomes related to drug absorption.

Incidence of hospitalization

The incidence of hospitalization was an outcome of interest in three studies (Albertson 1989; Kornberg 1991; Kulig 1985). Given the wide variety of toxic syndromes included in the individual studies, and the inability of laypeople to distinguish between ingested toxins, we considered a meta-analysis appropriate. The Peto OR was 1.17 (95% CI 0.69 to 1.98, 746 participants, 3 studies, P = 0.56), without any important heterogeneity (P = 0.15, I² = 47%; Analysis 7.5). We considered this evidence to be of very low certainty, due to limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence of ICU admission

One trial, Albertson 1989, reported the incidence of ICU admission (RR 1.38, 95% CI 0.44 to 4.38, 200 participants, 1 study, P = 0.58; Analysis 7.6). We considered this evidence to be of very low certainty, downgraded for limitations in study design, imprecision (low number of events or low sample size, and wide confidence intervals) and indirectness.

Summary for this comparison

Evidence from four studies suggests that adding syrup of ipecac to SDAC plus cathartics may make little difference for clinical improvement. On the other hand, we are uncertain about its impact on mortality, adverse events, clinical deterioration, hospitalization or ICU admission. Evidence was of low to very low certainty, downgraded for limitations in study design, imprecision and/or indirectness.

8. Syrup of ipecac versus syrup of ipecac (different doses)

We found one study using different types of syrup of ipecac, manufactured according to the American Pharmacopeia (USP) or the Australian Pharmaceutical Formulary (AFP) (Ilett 1977). More interestingly, this study also compared two different doses of the AFP syrup of ipecac: 15 mL or 30 mL, followed by 200 mL water. This study involved 120 participants presenting to the emergency department of a hospital with various intoxications.

Primary outcomes

Incidence of mortality

The identified study either did not collect or did not report on outcomes related to incidence of mortality.

Adverse events

The identified study either did not collect or did not report on outcomes related to adverse events due to the intervention.

Incidence and severity of symptoms of poisoning

The identified study either did not collect or did not report on outcomes related to incidence and severity of poisoning symptoms.

Secondary outcomes

Duration of symptoms

The identified study either did not collect or did not report on outcomes related to duration of poisoning symptoms.

Drug absorption

The identified study either did not collect or did not report on outcomes related to drug absorption.

Incidence of hospitalization

The identified study either did not collect or did not report on outcomes related to incidence of hospitalization.

Incidence of ICU admission

The identified study either did not collect or did not report on outcomes related to incidence of ICU admission.

Summary for this comparison

We identified one study that compared the use of different doses of syrup of ipecac (Ilett 1977), but it did not report any outcome of interest to our review.

B2. Cathartics

9. Single-dose activated charcoal plus cathartics versus single-dose activated charcoal alone

Two trials compared SDAC plus cathartics versus SDAC alone (James 1995; Sue 1994). Both trials studied children presenting to

the emergency department following various or unspecified toxic ingestions, requiring SDAC. See Appendix 3.

Primary outcomes

Incidence of mortality

The identified studies either did not collect or did not report outcomes related to incidence of mortality.

Adverse events

In Sue 1994 the only measured adverse event due to the intervention was lethargy during follow-up. Authors reported no cases of lethargy in the SDAC plus magnesium citrate group (50 participants) or in the SDAC group (14 participants). James 1995 recorded the incidence of participants vomiting upon receiving activated charcoal with or without sorbitol, magnesium citrate or magnesium sulphate. The pooled RR was 1.46 (95% CI 0.61 to 3.49, 116 participants, P = 0.39; Analysis 8.1). We considered the evidence to be of very low certainty, due to limitations in study design, imprecision (low number of events) and indirectness.

Incidence and severity of symptoms of poisoning

The identified studies either did not collect or did not report outcomes related to occurrence and severity of symptoms of poisoning.

Secondary outcomes

Duration of symptoms

The identified studies either did not collect or did not report outcomes related to symptom duration.

Drug absorption

The identified studies either did not collect or did not report outcomes related to drug absorption.

Incidence of hospitalization

Sue 1994 studied the incidence of hospitalization. Three participants required hospitalization in the group receiving SDAC plus either 4 mL/kg, 6 mL/kg or 8 mL/kg of magnesium citrate, versus one patient in the activated charcoal group (RR 0.84, 95% CI 0.09 to 7.46, 64 participants, P = 0.88; Analysis 8.2). The evidence was of very low certainty, downgraded for limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence of ICU admission

The identified studies did not report outcomes related to incidence of ICU admission.

Summary for this comparison

We are uncertain if adding SDAC to a cathartic has an effect on adverse events or hospitalization. The evidence was of very low certainty, downgraded for limitations in study design, imprecision and indirectness.

10. Single-dose activated charcoal plus different doses of cathartics

Sue 1994 assessed SDAC with different doses of cathartics. This trial studied 64 children presenting to the emergency department

following an unspecified toxic ingestion requiring SDAC. See Appendix 4.

Primary outcomes

Incidence of mortality

The identified study either did not collect or did not report outcomes related to incidence of mortality.

Adverse events

The only measured adverse event due to the intervention was lethargy during follow-up. Authors reported no cases of lethargy in any of the treatment groups (Table 3). We considered this evidence to be of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Incidence and severity of symptoms of poisoning

The identified study either did not collect or did not report outcomes related to incidence and severity of symptoms of poisoning.

Secondary outcomes

Duration of symptoms

The identified study either did not collect or did not report outcomes related to symptom duration.

Drug absorption

The identified study either did not collect or did not report outcomes related to drug absorption.

Incidence of hospitalization

No patient required hospitalization in the group receiving 4 mL/kg of magnesium citrate plus SDAC compared to one participant in the 6 mL/kg magnesium citrate plus SDAC group and two participants in the 8 mL/kg magnesium citrate plus SDAC group. When comparing 6 mL/kg or 8 mL/kg magnesium citrate versus 4 mL/kg, the ORs were 7.39 (95% CI 0.15 to 372.38, 32 participants, P = 0.32; Table 3) and 7.01 (95% CI 0.42 to 117.63, 34 participants, P = 0.18; Table 3), respectively. The RR when comparing 6 mL/kg to 8 mL/kg magnesium citrate was 1.78 (95% CI 0.18 to 17.80, 34 participants, P = 0.62; Analysis 9.1). We considered this to be evidence of very low certainty, due to limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence of ICU admission

The identified study either did not collect or did not report outcomes related to incidence of ICU admission.

Summary for this comparison

We are uncertain about the effects of higher doses of magnesium citrate combined with SDAC, compared to lower doses combined with SDAC, with respect to the incidence of adverse events or hospitalization. These results were of very low certainty, downgraded for limitations in study design, imprecision and indirectness.

11. Single-dose activated charcoal plus different types of cathartics

One trial compared SDAC plus different types of cathartics, namely sorbitol, magnesium citrate and magnesium sulphate (James 1995). This trial studied 119 children who ingested a variety of toxins (analgesics, anticonvulsants, antihistamines and decongestants, asthma therapies, automotive products, cardiovascular drugs, gastrointestinal preparations, insecticides, mushrooms, psychotropic drugs, rodenticides, topicals, or miscellaneous drugs). See Appendix 5.

Primary outcomes

Incidence of mortality

The identified study either did not collect or did not report outcomes related to incidence of mortality.

Adverse events

Emesis occurred in 13 of 32 children receiving SDAC plus sorbitol; 6 of 33 children receiving SDAC plus magnesium citrate, and 4 of 23 children receiving SDAC plus magnesium sulphate.

When comparing sorbitol with magnesium sulphate, the RR was 2.34 (95% CI 0.87 to 6.25, 55 participants, P = 0.09; Analysis 10.1). Sorbitol versus magnesium citrate resulted in an RR of 2.23 (95% CI 0.97 to 5.16, 55 participants, P = 0.06; Analysis 10.2). For magnesium sulphate versus magnesium citrate, the RR is 0.96 (95% CI 0.30 to 3.01, 55 participants, P = 0.94; Analysis 10.3). We considered this evidence to be of very low certainty, due to limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence and severity of symptoms of poisoning

The identified study either did not collect or did not report outcomes related to incidence and severity of symptoms of poisoning.

Secondary outcomes

Duration of symptoms

The identified study either did not collect or did not report outcomes related to symptom duration.

Drug absorption

The identified study either did not collect or did not report outcomes related to drug absorption.

Incidence of hospitalization

The identified study either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

The identified study either did not collect or did not report outcomes related to incidence of ICU admission.

Summary for this comparison

Only one study assessed the effect of different types of cathartics in combination with SDAC in the treatment of poisoning. The only relevant outcome measured is incidence of emesis as an adverse event, for which any effect of using different types of cathartics

is uncertain. Evidence is of very low certainty, downgraded for limitations in study design, imprecision and indirectness.

C. Combined first aid interventions that limit uptake and promote evacuation of the poison from the gastrointestinal tract

12. Single-dose activated charcoal plus cathartic plus hospital intervention versus hospital intervention alone

One study compared SDAC plus a cathartic plus hospital interventions versus hospital interventions alone (Passeron 1989). Passeron 1989 included participants presenting with a confirmed overdose of benzodiazepines, barbiturates or imipramine. All participants in this study received gastric lavage prior to the SDAC plus sorbitol or no additional intervention. See Appendix 6.

Primary outcomes

Incidence of mortality

The identified study either did not collect or did not report outcomes related to incidence of mortality.

Adverse events

The included study reported the incidence of vomiting (Passeron 1989). The Peto OR was 9.94 (95% CI 1.52 to 65.02, 32 participants; Analysis 11.1). The level of evidence was very low, downgraded due to limitations in study design, imprecision (low number of events and wide confidence intervals) and indirectness.

Incidence and severity of symptoms of poisoning

Passeron 1989 monitored participants' symptoms using the Glasgow Coma Scale. They did not report any numeric data but reported no difference for the course of the Glasgow Coma Scale scores between treatments (P = 0.49). The evidence was of very low certainty, downgraded for limitations in study design, imprecision due to a lack of data and indirectness.

Secondary outcomes

Duration of symptoms

The identified study either did not collect or did not report outcomes related to symptom duration.

Drug absorption

Passeron 1989 measured drug levels in their participants, but did not report any of our pre-defined outcomes of interest (AUC, C_{max}, T_{max}), so we could not make a reliable estimate of effect on drug absorption.

Incidence of hospitalization

The identified study either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

The identified study either did not collect or did not report outcomes related to incidence of ICU admission.

Summary for this comparison

We found only evidence of very low certainty (downgraded for limitations in study design, imprecision and indirectness) concerning the use of SDAC plus a cathartic, in adjuvant to

established hospital treatments. Thus we are uncertain about the effect on Glasgow Coma Scale scores or incidence of vomiting.

13. Multi-dose activated charcoal plus cathartic plus hospital intervention versus hospital intervention alone

One study in 14 participants compared MDAC plus magnesium sulphate as an adjuvant to oral N-acetylcysteine versus N-acetylcysteine alone for paediatric paracetamol overdose (Montoya-Cabrera 1999). See Appendix 7.

Primary outcomes

Incidence of mortality

The identified study either did not collect or did not report outcomes related to incidence of mortality.

Adverse events

Montoya-Cabrera 1999 reported that no adverse events occurred in any treatment group (Table 3). This is evidence of very low certainty, downgraded for limitations in study design, imprecision (low number of events) and indirectness.

Incidence and severity of symptoms of poisoning

The identified study either did not collect or did not report outcomes related to occurrence and severity of poisoning symptoms.

Secondary outcomes

Duration of symptoms

The identified study either did not collect or did not report outcomes related to symptom duration.

Drug absorption

Montoya-Cabrera 1999 measured $T_{1/2}$ of paracetamol in the plasma, reporting a decrease (P < 0.05; Table 3). However, they failed to report any measure of spread, so we cannot report any summary estimate with 95% CI. We consider the evidence to be of very low certainty due to limitations in study design, imprecision (low sample size and lack of data) and indirectness.

Incidence of hospitalization

The identified study either did not collect or did not report outcomes related to incidence of hospitalization.

Incidence of ICU admission

The identified study either did not collect or did not report outcomes related to incidence of ICU admission.

Summary for this comparison

We identified one study, which provided evidence of very low certainty (downgraded for limitations in study design, imprecision and indirectness) (Montoya-Cabrera 1999). Any effect on the incidence of adverse events or plasma half-life of paracetamol after receiving MDAC in adjuvant to oral administration of N-acetylcysteine, compared to oral administration of N-acetylcysteine alone is uncertain.

D. First aid interventions that neutralize or dilute the poison

We identified no studies comparing interventions aiming at neutralizing or diluting orally ingested poisons in a patient setting.

DISCUSSION

Summary of main results

Out of a total of 11,582 potentially relevant references, we identified 24 studies reported in 31 publications. All but one study took place in a hospital setting (Wax 1999 was in a pre-hospital setting). A total of 7099 participants were randomized to different treatment groups.

A. First aid interventions that limit or delay the absorption of the poison in the body

Activated charcoal

A commonly used intervention in poisoning is activated charcoal. Due to its enormous surface area it can adsorb large quantities of drugs, thus preventing the absorption of the poison by the body. Included studies made different comparisons, either using single-dose activated charcoal (SDAC) alone, combined with other pre-hospital treatments, or in adjuvant to hospital interventions. Furthermore, multi-dose activated charcoal (MDAC) was used in adjuvant to hospital interventions.

We found very low-certainty evidence from two studies, involving 476 participants and comparing single-dose activated charcoal to no intervention, which is our main comparison (Merigian 1990; Underhill 1990). These studies included participants with unspecified exposures in Merigian 1990 or paracetamol overdoses in Underhill 1990. Any effect on the incidence of adverse events, clinical deterioration or ICU admission is uncertain. See Summary of findings for the main comparison.

Seven trials, providing evidence of low to very low certainty and including 5383 participants, investigated the effect of SDAC in adjuvant to established hospital interventions such as supportive treatment and in most cases also gastric lavage (Comstock 1982; Cooper 2005; Crome 1983; Eddleston 2008; Hultén 1988; Merigian 2002; Roberts 2006). All but three studies either did not specify a toxic syndrome or recruited participants with different toxic syndromes (Crome 1983; Hultén 1988; Roberts 2006). There may be little or no difference in the incidence of mortality or the need for and length of intubation. We are uncertain about the effects of SDAC in addition to hospital treatments with regard to adverse events, drug absorption and incidence of hospitalization or ICU admission. See Summary of findings 2.

Five trials including 3568 participants compared MDAC versus SDAC, all in adjuvant to hospital interventions (Behnoush 2009; Brahmi 2006; De Silva 2003; Eddleston 2008; Roberts 2006). Two trials included participants with carbamazepine overdose (Behnoush 2009; Brahmi 2006), and two trials studied participants with yellow oleander poisoning (De Silva 2003; Roberts 2006). Eddleston 2008 included participants with different types of overdose, including yellow oleander and pesticide poisoning. There were some discrepancies between studies, preventing us from drawing any conclusions regarding incidence of mortality. This is evidence of very low certainty. In addition, low-certainty evidence suggests that MDAC may result in decreased incidence of ICU admissions and an increase in abdominal discomfort or

diarrhoea, but it may have no influence on the need for intubation. Furthermore, we are uncertain about the effects of MDAC on drug absorption or length of intubation, evidence of very low certainty. See Summary of findings 3.

We identified one study, involving 34 participants, with very low-certainty evidence that compared SDAC with syrup of ipecac in participants with anti-inflammatory, analgesic or psychotropic drug overdose (Amigó Tadín 2002). We are uncertain about the effect of SDAC versus ipecac on the incidence of adverse events or Glasgow Coma Scale scores. See Summary of findings 4.

We identified three studies comparing MDAC in adjuvant to hospital intervention versus hospital intervention alone in 3121 participants (Bouget 1989; Eddleston 2008; Roberts 2006). This low- to very low-certainty evidence suggests there may be no difference in the incidence of mortality, symptoms of intoxication or length of intubation, while we are uncertain about its effects on pharmacokinetic parameters. See Summary of findings 5.

None of the above-mentioned evidence could show added value for the use of activated charcoal, either administered as a single dose or as multiple doses, or in adjuvant or not to hospital interventions.

Body position

Another possible intervention to slow down the uptake of the poison is a certain body position. The theory is that placing a patient on the left lateral decubitus position would allow the gastric content to stay in the greater curvature of the stomach, due to the combination of gravity and the anatomy of the stomach, which might slow down the rate of absorption of the poison. However, we did not identify any studies performed in poisoning participants that compared different kinds of body position.

B. First aid interventions that evacuate the poison from the gastrointestinal tract

Vomiting or accelerated defecation might induce the quick evacuation of the poison from the gastrointestinal tract. Interventions that might obtain this effect are emetics, which induce vomiting, or cathartics, for the acceleration of defecation.

Emetics

Five included studies looked at the effectiveness of syrup of ipecac as a first aid measure for poisoning.

One study including 103 participants provided evidence of low certainty on the use of ipecac versus no intervention in asymptomatic participants with toxic berry ingestion (Wax 1999). This study took place in a pre-hospital setting and reported no clinical outcomes. While there may be little or no difference in emergency department referral, there may be an increase in adverse events. See Summary of findings 6.

Four studies, involving 1240 participants, assessed the addition of syrup of ipecac to SDAC plus a cathartic (Albertson 1989; Kornberg 1991; Kulig 1985; Pond 1995). All studies either did not specify or included multiple types of overdose. Low-certainty evidence suggests there may be little or no difference in the incidence of clinical improvement. On the other hand, we are uncertain about any effect on the incidence of mortality, adverse events, clinical deterioration, hospitalization or ICU admission. See Appendix 2.

We identified one study with 120 participants comparing different doses of ipecac (Ilett 1977), but it did not report any outcomes of interest.

One study compared syrup of ipecac versus SDAC. We describe this study above (interventions that limit or delay the absorption of the poison in the body). See Summary of findings 4.

None of the evidence on the use of syrup of ipecac as a first aid intervention shows any benefit, and it may even cause harm.

Cathartics

Cathartics are often used in combination with activated charcoal, where activated charcoal is used to adsorb the poison and the cathartic to accelerate the evacuation from the gastrointestinal tract. We identified two studies in 183 participants that looked at the combination of different types or doses of cathartic with SDAC in children with unspecified or various intoxications (James 1995; Sue 1994).

These trials provided evidence of very low certainty comparing the use of SDAC plus a cathartic versus SDAC alone in either unspecified or multiple toxic syndromes. We are uncertain whether adding a cathartic to the treatment influences the incidence of adverse events or the incidence of hospitalization. See Appendix 3.

Sue 1994 assessed SDAC plus different doses of magnesium citrate in 64 participants, but we are uncertain whether this would result in a difference regarding the incidence of hospitalization. See Appendix 4.

James 1995 studied the effects of different types of cathartics (sorbitol, magnesium citrate or magnesium sulphate) in combination with SDAC, in 119 participants. We are uncertain whether a different type of cathartic in adjuvant to SDAC influences the incidence of vomiting as an adverse event. See Appendix 5.

In summary, we did not identify any trials that looked at the use of cathartics alone compared with no intervention. Cathartics were always used in combination to SDAC. From the limited evidence available, we are not able to draw conclusions regarding the use of cathartics in addition to SDAC.

C. Combinations of first aid interventions

One study including 32 participants looked at the effects of combining SDAC with cathartics as an adjuvant to hospital intervention, compared to hospital intervention alone in participants with overdoses of benzodiazepines, barbiturates or imipramine (Passeron 1989). The study provided evidence of very low certainty, so we are uncertain about the impact of adding SDAC plus cathartics in adjuvant to a hospital intervention on Glasgow Coma Scale scores or the incidence of vomiting. See Appendix 6.

One study in 14 participants used MDAC in combination with magnesium sulphate as a cathartic, in adjuvant to hospital treatment (Montoya-Cabrera 1999). The evidence of very low certainty precluded us from drawing conclusions about the effects of MDAC and magnesium sulphate in adjuvant to hospital treatments on the plasma half-life of paracetamol. See Appendix 7.

D. First aid interventions that neutralize or dilute the poison

We did not identify any studies in poisoning patients that looked at the effects of commonly used home remedies such as drinking milk, water, vinegar or citrus juice to neutralize or dilute the poison.

Overall completeness and applicability of evidence

The objective of this review was to assess the effects of pre-hospital interventions, alone or in combination, that laypeople could feasibly provide victims of acute oral poisoning before professional help arrives. We identified only one study from a pre-hospital setting (Wax 1999). As we anticipated that this would be the case in advance, we also included studies performed in a hospital setting as indirect evidence. Furthermore, half of the studies compared the intervention of interest in adjuvant to a hospital intervention versus hospital interventions alone. These considerations limit the applicability of our findings.

With regard to the interventions of interest, about two-thirds of the identified studies looked at SDAC and MDAC alone or in combination with cathartics, and sometimes in adjuvant to hospital treatment. We identified six studies assessing syrup of ipecac. We found little evidence on the use of cathartics, and in the two studies we did identify cathartics were used in adjuvant to another treatment (i.e. SDAC), making it difficult to make a judgment on the use of cathartics by themselves for oral poisoning. Finally, we found no studies of the effect of body position or interventions that might dilute or neutralize the poison, such as drinking water or milk.

The 24 identified studies described a wide range of outcomes. However, the primary outcomes of interest, mortality, severity of symptoms due to poisoning and adverse events, were very variably and often incompletely reported. Useable data on these outcomes were thus limited. This also precluded combining the different interventions in this review in a network meta-analysis (NMA), which would have allowed us to compare the relative efficacy of different interventions and potentially rank the interventions for efficacy. We will perform an NMA for future updates of this review, if more useable data becomes available.

Furthermore, most studies were over 10 years old, with the oldest study being performed in 1977 (Ilett 1977). Only two studies took place in the past decade (Behnoush 2009; Eddleston 2008).

A major limitation in most of the identified studies is the substantial heterogeneity of the included participants. This might obscure potential benefits in subgroups of participants, for example participants with severe poisoning, specific toxic syndromes or those presenting early (Juurlink 2015). On the other hand, in a first aid setting it might often be unclear what type of patient a caregiver is dealing with, with regard to the type, dose and timing of intoxication, further complicating conclusions with respect to the lay setting.

Overall, the identified evidence is scarce and of low to very low certainty, which precludes any firm conclusions about the added value of any of the first aid interventions discussed in this review. However, almost all of these studies were performed in a hospital setting, which means there is a delay in presentation and thus treatments are started at a later time than when given in a home setting. It could therefore be possible that treatments were not effective because of their delayed administration.

In addition, evidence is too scarce to be able to draw conclusions about the safety of most of the first aid interventions. The exception is syrup of ipecac, for which low-certainly evidence suggests that the number of complications increases when using it compared to no intervention.

Quality of the evidence

A key methodological limitation in the included studies is that most studies used inappropriate or unclear methods of randomization. Furthermore, most studies reported outcomes poorly, and the reporting format was highly heterogeneous. This makes the studies difficult to compare with one another. The variation between and within studies with respect to the population further complicates the comparison of different studies.

First aid interventions that limit or delay the absorption of the poison in the body

For most of the comparisons including single- or multi-dose activated charcoal, the evidence is of low to very low certainty. In most cases, we downgraded the evidence for indirectness (since most studies were performed in a hospital setting), imprecision (limited sample size, low number of events and/or wide confidence intervals) and limitations in study design.

In the comparison of SDAC versus MDAC (both in adjuvant to hospital interventions), we identified two studies at low risk of bias; however, there was inconsistency between the studies' findings, which makes it difficult to draw any conclusions. There is no clear cause of this inconsistency, but possible explanations might be that De Silva 2003 included participants up to 72 h after poison ingestion, whereas Eddleston 2008 included participants only up to 24 h after ingestion. Furthermore, Eddleston 2008 included less severely poisoned participants than De Silva 2003 (Glasgow Coma Scale of less than 13).

First aid interventions that evacuate the poison from the gastrointestinal tract

For interventions that promote the evacuation of the poison from the gastrointestinal tract, we found the most evidence on the use of syrup of ipecac. However, all studies were at high risk of selection bias, and most were at high or unclear risk of detection bias. We further downgraded studies due to imprecision and indirectness, leading to low or very low certainty evidence.

The evidence on the use of cathartics was limited and of very low certainty due to a high risk of reporting bias, indirectness and imprecision. The identified studies always used cathartics in combination with other interventions, making it difficult to draw conclusions about cathartics alone as a treatment for oral poisoning.

First aid interventions that neutralize or dilute the poison

There are no available data that we identified on interventions that neutralize or dilute the poison.

Potential biases in the review process

This review intended to assess interventions that are feasible for laypeople to use in situations of oral poisoning. This means that the interventions should be feasible to use in a pre-hospital setting by people without any medical knowledge. According to these criteria,

we excluded interventions such as gastric lavage or intravenous drug administrations.

Most identified studies took place in a hospital setting, which means that we had to downgrade the level of evidence due to indirectness. Only one included study was in a pre-hospital community setting, but it included only asymptomatic poisoning patients.

Although the interventions were mostly in a hospital setting, we included only studies that used interventions feasible by laypeople. We only allowed comparisons with hospital interventions if the treatment group received the same hospital interventions in adjuvant to the possible first aid treatment under investigation.

We did not include the many available volunteer studies. These are studies in which healthy volunteers receive a drug in a therapeutic or supratherapeutic dose in an attempt to simulate oral poisoning, in a controlled setting such as a laboratory environment, mostly without co-ingestion of other drugs or alcohol, on an empty stomach. We believed this was even more indirect than including studies performed in actual oral poisoning patients, although they were performed in a hospital setting.

As mentioned earlier, most studies were over 10 years old, with the oldest study from 1977. Only two studies took place within 10 years of our literature search. Many of the studies were poorly reported: data were missing, and our attempts to contact the authors were often unsuccessful because no contact details were available, authors did not respond, or data were no longer available. This could introduce a bias on the completeness of the data and the risk of bias assessment, leading to perhaps a more strict judgment of bias for some studies.

Agreements and disagreements with other studies or reviews

An existing Cochrane Review on interventions for paracetamol (acetaminophen) overdose included not only possible first aid interventions such as activated charcoal or syrup of ipecac, but also hospital interventions such as gastric lavage, charcoal haemoperfusion, antidotes such as N-acetylcysteine or cimetidine, and liver transplantations (Chiew 2018). The review included randomized controlled trials as well as observational studies, and studies performed in healthy volunteers as well as in patients. In our review, the focus is on first aid interventions feasible for laypeople. This excludes all types of hospital interventions. Furthermore, we did not focus on a specific toxin, and since sufficient studies in patients were available, we decided to exclude studies performed in healthy volunteers. We agree with the conclusions of Chiew 2018 that the use of activated charcoal seems a safer option than syrup of ipecac to reduce uptake, although research still needs to demonstrate a clear clinical benefit.

There might be some overlap with the different position papers published on the use of SDAC (American Academy of Clinical Toxicology 2005), MDAC (American Academy of Clinical Toxicology 1999), cathartics (American Academy of Clinical Toxicology 2004), and syrup of ipecac (Höjer 2013). These papers give a comprehensive overview of the interventions and discuss the published literature, from preclinical to clinical research. However, most are out of date, and it is not clear if the literature search was systematic. Our systematic review does highlight that in the decade preceding publication, there has been very little research on this important topic.

Furthermore, the position papers only give a description of the different identified studies, whereas in our review we combined studies in a meta-analysis where possible, to give an overall effect size. In any case, our conclusions are largely similar: there is insufficient evidence for a clinical benefit and thus for the routine use of any of the investigated treatments. Few studies have been published since the publication of these position papers, and while our review includes them, all fail to show a clear clinical benefit for the use of these first aid treatments in a hospital setting. However, one important difference is that the recommendations made in these position papers were designed for a professional care setting. The relevance for a pre-hospital setting remains unclear.

A systematic literature search and meta-analysis on the effect of activated charcoal in healthy volunteers showed that administration of activated charcoal was most effective when administered immediately after drug intake, but it was still effective up until four hours after drug ingestion (Jürgens 2009). There was no information on adverse events due to the intervention. This meta-analysis demonstrates the theoretical capacity of activated charcoal to reduce uptake of a variety of toxins. However, the actual clinical benefit for oral poisoning patients remains speculative, as demonstrated by the studies included in our review, which fail to show a clear clinical benefit. Reasons for the discrepancy between data collected from healthy volunteers and actual patients might include the time passed between ingestion of the drugs and the start of the treatment. Also, the meta-analysis looked at activated charcoal as the only treatment. It did not assess any combination treatments, such as activated charcoal plus a cathartic. Furthermore, the controlled setting where studies in healthy volunteers take place excludes certain confounding variables, for example ingesting the drugs with alcohol, intake of a cocktail of different kinds of drugs or not knowing which drugs were taken. These considerations imply that the use of activated charcoal is still a therapeutic option in emergency departments, but clinicians should carefully consider its use for individual patients (Juurlink 2015). From the available evidence, it is unclear whether a layperson would be capable of making these considerations in a pre-hospital setting.

AUTHORS' CONCLUSIONS

Implications for practice

We are unsure about the effects of activated charcoal, syrup of ipecac or cathartics for pre-hospital management by laypeople of acute oral poisoning, due to the low- or very low-certainty evidence. Data mostly came from emergency care departments, where the added value of first aid interventions is uncertain. Given the indirectness of these results, it is not possible to draw any conclusions concerning the use of these interventions for the pre-hospital setting.

Implications for research

There are many studies available on the use of activated charcoal, cathartics, syrup of ipecac or combinations of these interventions. Studies are performed either in oral poisoning patients or in healthy volunteers, mostly in a healthcare or controlled setting. However, there is very little up-to-date evidence. Researchers may

feel hampered by practical issues to further investigate these interventions; nevertheless, the most recent studies show that high methodological quality can be feasible and ethical. The identified evidence, however, is indirect.

On the other hand, the clinical benefit of the one recommendation that is being made in practice in a pre-hospital setting (IFRC 2016), the use of the left lateral decubitus position, remains to be demonstrated. If researchers are designing future studies on the effectiveness of first aid measures for acute oral poisoning, these could take place in a pre-hospital setting, for example by collaborating with poisoning centres, to avoid the delay that is inherent to hospital studies. This delay precludes firm conclusions about interventions whose effectiveness decreases over time, as is clearly the case for interventions that try to limit the uptake of a poisonous substance.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Albertson 1989

Methods	*Study design*: randomized controlled trial
	Study duration: 24 months ending December 1987
	Setting: emergency department (ED) at UC Davis Medical Center
	Country: USA
	Number of individuals randomized: 200
	Number of individuals receiving the intervention: 93
	Number of individuals receiving the control: 107
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: 113 women, 87 men
	Age: 30.1 (SEM 0.8), range 18-77 years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: all participants with mild or moderate oral overdose, 56% had mixed overdoses, most frequently with ethanol, timing could not be reliably obtained in most participants
	Inclusion criteria: awake with gag reflex, > 18 years, cooperative
	Exclusion criteria: rapidly deteriorating level of consciousness, previous vomiting, received ipecac syrup at home or en route, ingested substance with contraindication for ipecac syrup, ingested strong acids or bases, camphor, volatile petroleum distillates and strychnine, ingested large amounts of iron and lithium alone
Interventions	*Intervention arm*:
	Type: syrup of ipecac followed with activated charcoal-sorbitol after vomiting subsided
	Timing:
	Syrup of ipecac: no information
	AC-sorbitol: after induced vomiting
	Dose: 30 mL ipecac syrup + 1 g/kg AC (50 g AC-sorbitol-water suspension
	Frequency: 1× ipecac unless no response then repeated after 30 min + 1× AC
	Integrity: no information
	Control arm:
	Type: activated charcoal-sorbitol
	Timing: no information
	Dose: 1 g/kg AC (50 g AC-sorbitol-water suspension)
	Frequency: 1×

Albertson 1989 *(Continued)*

	Integrity: no information
Outcomes	*Type (unit)*:
	Mean time in the emergency department (h) (see Table 4)
	Proportion requiring hospitalization
	Number of days hospitalized (see Table 4)
	Proportion admitted to the intensive care unit
	Number of days in ICU (see Table 4)
	Proportion of complications
	Timing: during time in the hospital (early)
Funding	No information
Notes	75% had toxicology screen done but was not a criterion for inclusion or exclusion

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "were randomized by hospital unit numbers to two treatment groups"
		Comment: not an adequate randomisation method
Allocation concealment (selection bias)	High risk	Quote: "were randomized by hospital unit numbers to two treatment groups"
		Comment: allocation scheme does not allow allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied (e.g. mean time spend in the emergency department)
Incomplete outcome data (attrition bias) All outcomes	Low risk	No specific information, but no failure to adhere to intervention reported
Selective reporting (reporting bias)	High risk	No assessment of symptom severity
Other bias	High risk	Quote: "Most patients (75%) had partial or complete toxicological analysis of blood and/or urine performed, although this was not a requirement of the study."
		Comment: for 25% of the participants, actual poisoning was not verified by means other than history.

Amigó Tadín 2002

Methods	*Study design*: randomized controlled trial
	Study duration: 11 December 2000 to 12 March 2001
	Setting: emergency department of a tertiary healthcare facility (El Hospital Clinic, Barcelona)
	Country: Spain
	Number of individuals randomized: 34
	Number of individuals receiving the intervention: 21
	Number of individuals receiving the control: 13
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*:
	Ipecac: 17 females, 4 males
	AC: 10 females, 3 males
	Age:
	Ipecac: 35 (SD 13) years
	AC: 27 (SD 6) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants presenting at the emergency department with an oral overdose of either anti-inflammatory drugs, analgesics or psychotropic drugs. 91% were psychotropics, mostly benzodiazepines, followed by tricyclic antidepressants. In 35% of cases, more than 1 drug was taken. 18% were taken with alcohol.
	Selection criteria:
	Inclusion criteria: > 15 years and Glasgow score > 12
	Exclusion criteria: participants with a medical indication for gastric lavage or if it had previously been performed by a medical service in an out-of-hospital setting. Presenting more than 2 h after intoxication unless they had taken antidepressants, neuroleptics, salicylates or opioids in which the interval was extended to 4 h. Participants for whom, due to their potential severity, was presumed that 1-2 doses of SOI or AC would be insufficient to effectively decontaminate the digestive tract
Interventions	*Intervention arm*:
	Type: syrup of ipecac
	Timing: 8.65 (SD 8.4) min after arriving at the ED or 113.46 (SD 80.29) min after ingestion
	Dose: 30 mL, followed by 240 mL of water
	Frequency: 1×
	Integrity: dose was repeated after 20 minutes if no vomiting occurred in that time
	Time to vomiting: 32 (SD 25.17) min, mean number of vomiting episodes: 2.05 (SD 1.68). 38% of vomits contained rests of tablets. 3 people did not vomit.
	Control arm:
	Type: activated charcoal

Timing: 10.68 (SD 9.48) min after arriving at the ED or 112.35 (SD 81.48) min after ingestion

Dose: 25 g in 200 mL of water

Frequency: 1×

Integrity: in order to mask the black color of the AC and so that its oral administration did not pose problems of acceptability, it was given in the same jar in which it is marketed or in a glass with a cane

Outcomes	*Type (unit)*: Mean arterial blood pressure (mmHg) Heart rate (bpm) Breathing rate (breaths/min) Glasgow Coma Scale score Length of stay ED (min) (see Table 4) Workload nurses (data not extracted) Adverse events *Timing*: Clinical parameters: 1 h after initial assessment of patient (early) Rest: during ED stay (early)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients entering on even days receives syrup of ipecac and patients entering on uneven days received activated charcoal." Comment: no adequate randomization
Allocation concealment (selection bias)	High risk	Quote: "Patients entering on even days receives syrup of ipecac and patients entering on uneven days received activated charcoal." Comment: randomization scheme does not allow allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied (e.g. Glasgow Coma Scale assessment)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "The rest were excluded because they had a Glasgow coma score < 12, did not meet the inclusion criteria or because caregivers were not able to complete the forms".

Amigó Tadín 2002 *(Continued)*

		Comment: of the 97 potentially eligible participants, only 34 were included, due to justified reasons as "Glasgow coma score <12" or "not meeting inclusion criteria", but also due to staff business. Not clear how many participants were lost because of this
Selective reporting (reporting bias)	Low risk	No indication of a risk of reporting bias
Other bias	Low risk	No indication of other risk of bias

Behnoush 2009

Methods	*Study design*: randomized controlled trial
	Study duration: July 2003 to September 2004
	Setting: hospital setting (poisoning ward of the Loghman Hospital, Tehran)
	Country: Iran
	Number of individuals randomized: 68
	Number of individuals receiving the intervention: 38
	Number of individuals receiving the control: 30
	Number of individuals lost to follow-up: unclear, as loss to follow-up was considered an exclusion criterion for the study
	Sample size calculated: yes, but methods are not clearly reported: "The sample size was measured according to the descriptive studies formula, and the P value was calculated based on the number of controls with carbamazepine poisoning in Loghman Hospital, in previous years."
Participants	*Sex*: 28 males and 40 females
	Age: 24.2 years, range 13-65 years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants admitted to the poisoning ward with history of carbamazepine poisoning:
	Dose average (range): 6.8 g (1.2-24 g)
	Delay between drug intake and admission average (range): 7.44 h (0.5 h to 15 h)
	Inclusion criteria: poisoning confirmed by clinical examination and paraclinical tests
	Exclusion criteria: taken other drugs or unknown drugs, hospitalization not needed, left hospital before completion of treatment, not possible to confirm poisoning by carbamazepine
Interventions	*Intervention arm*:
	Type: MDAC via nasogastric tube + supportive treatment (including gastric lavage)
	Timing: every 4 h
	Dose: 100 g AC per dose
	Frequency: several, but unknown number of doses

Behnoush 2009 *(Continued)*

	Integrity: no information
	Control arm:
	Type: SDAC via nasogastric tube + supportive treatment (including gastric lavage)
	Timing: no information provided, presumably after poisoning confirmation
	Dose: not specified, but likely 100 g AC
	Frequency: 1×
	Integrity: no information
Outcomes	*Type (unit)*: duration of hospitalization (h) (see Table 4)
	Timing: no information
Funding	No information
Notes	All 8 ICU participants, with grade III or IV level of unconsciousness received the multi-dose treatment, thus seem not to have been randomized and were therefore not included in the analysis of hospitalization duration

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "In all patients admitted to I.C.U. and 30 patients of the ward, multiple doses of charcoal were administered, whereas the resting 30 patients -who were chosen randomly- received single doses of charcoal" Comment: not enough information to make a judgment
Allocation concealment (selection bias)	Unclear risk	Quote: "In all patients admitted to I.C.U. and 30 patients of the ward, multiple doses of charcoal were administered, whereas the resting 30 patients -who were chosen randomly- received single doses of charcoal" Comment: not enough information to make a judgment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "The following patients were excluded from the study: those who left the hospital before the treatment process was completed" Comment: participants that did not complete the treatment process were excluded and no data is available on the number of people
Selective reporting (reporting bias)	High risk	Occurrence of complications not clearly described: unclear in which group they occurred. Drug and symptom monitoring are crucial outcomes that are lacking in this study. Especially for symptom monitoring, which was described as being the criterion for hospital discharge, this is problematic.
Other bias	Low risk	No other risk of bias detected

Bouget 1989 *(Continued)*

Methods	*Study design*: randomized controlled trial
	Study duration: one month
	Setting: hospital setting (emergency department of a regional hospital)
	Country: France
	Number of individuals randomized: 36
	Number of individuals receiving the intervention: 19
	Number of individuals receiving the control: 17
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*:
	MDAC group: 16 female and 3 male
	Control group: 12 female and 5 male
	Age:
	MDAC group: 31 (SD 3.6) years
	Control group: 30 (SD 3.5) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants presenting with a deliberate overdose of benzodiazepines, with or without concomitant alcohol ingestion
	Inclusion criteria: overdose of benzodiazepines of any sort, with or without alcohol
	Exclusion criteria: pregnant women, participants < 18 years old, concomitant ingestion of other drugs
Interventions	*Intervention arm*:
	Type: MDAC (Carbomix) + supportive treatment including gastric lavage and infusion of a an isotonic solution (5% glucose, enriched with 2 g/L KCl & 4 g/L NaCl)
	Timing: after gastric lavage, and after 4 h, 8 h, 12 h
	Dose: 50 g
	Frequency: 4×
	Integrity: no information
	Control arm:
	Type: supportive treatment including gastric lavage and infusion of a an isotonic solution (5% glucose, enriched with 2 g/L KCl and 4 g/L NaCl)
	Timing: gastric lavage: upon admission. Infusion: every 12 h
	Dose:
	Gastric lavage: 15 L

Bouget 1989 *(Continued)*

Infusion: 1 L/time

Frequency:

Gastric lavage: 1×

Infusion: every 12 h

Integrity: no information

Outcomes	*Type (unit)*:
	Glasgow Coma Scale score
	Heart rate
	Blood pressure
	Diuresis
	Temperature
	Benzodiazepine concentration
	Timing:
	At 0 h and 12 h after intervention (early)
	Blood samples were drawn every 4 h until discharge (early)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "By drawing of a lot" Comment: adequate method of randomisation
Allocation concealment (selection bias)	Unclear risk	Quote: "By drawing of a lot" Comment: not enough information to make a judgment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect certain outcomes at study (e.g. Glasgow Coma Scale scores)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information about incomplete outcomes
Selective reporting (reporting bias)	High risk	Outcomes are not reported in such a way that any interpretation is possible

Bouget 1989 *(Continued)*

Other bias	Low risk	No other risk of bias detected

Brahmi 2006

Methods	*Study design*: randomized controlled trial
	Study duration: January to June 2004
	Setting: 8 men and 4 women
	Country: hospital setting (intensive care and toxicological unit)
	Number of individuals randomized: 12
	Number of individuals receiving the intervention: 6
	Number of individuals receiving the control: 6
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: 8 men and 4 women
	Age: 27.6 (SD 12.2) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants admitted with a history of carbamazepine (CBZ) poisoning. Participants did not receive gastric lavage and received the same symptomatic and supportive treatment, as needed.
	Poisoning symptoms at admission:
	SAPS II score: 16.37 (SD 8.46)
	APACHE II score:
	8 (SD 3.96)
	Glasgow coma score of the comatose participants (6):
	8.28 (SD 1.6)
	CBZ concentration:
	29.42 (SD 6.68) mg/L
	Inclusion criteria: history of CBZ ingestion, clinical features of poisoning, and laboratory findings using gas chromatography
	Exclusion: children, mixed poisoning
Interventions	*Intervention arm*:
	Type: MDAC via nasogastric tube
	Timing: every 6 h
	Dose: 50 g AC
	Frequency: variable, until carbamazepine blood levels drop below 12 mg/L

Brahmi 2006 *(Continued)*

Integrity: no information

Control arm:

Type: SDAC via nasogastric tube

Timing: no information

Dose: 1 g/kg AC

Frequency: 1×

Integrity: no information

Outcomes	*Type (unit)*:
	C_{max} (mg/L)
	$T_{1/2}$ (h)
	Ventilation required
	Duration of ventilation (h)
	Duration of coma (h)
	Length of stay (h) (see Table 4)
	Timing: blood levels measured every 3 h until the peak and then every 6 h. (intermediate)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Once CBZ poisoning was retained, no gastric lavage was done, and patients were randomized in 2 groups." Comment: not enough information to make a judgment
Allocation concealment (selection bias)	Unclear risk	Quote: "Once CBZ poisoning was retained, no gastric lavage was done, and patients were randomized in 2 groups." Comment: not enough information to make a judgment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect certain outcomes studied (e.g. decision to discharge)
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up described

Brahmi 2006 *(Continued)*

Selective reporting (re-porting bias)	High risk	No AUC or potential adverse events reported
Other bias	High risk	A clinical difference is suspected between intervention and control group, based on the divergent carbamazepine kinetics

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Comstock 1982

Methods	*Study design*: randomized controlled study
	Study duration: October 1975 to June 1976
	Setting: hospital (emergency department of the Ben Taub hospital, Houston, Texas)
	Country: USA
	Number of individuals randomized: 339
	Number of individuals receiving the intervention: 131
	Number of individuals receiving the control: 208
	Number of individuals lost to follow-up:277 at the start of follow-up, 308 at the 3-5 h sample
	Sample size calculated: no information
Participants	*Sex*: no information
	Age: no information
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants presenting with illness associated with acute oral drug overdose, and at the discretion of the attending physician selected for gastric lavage.
	Of these, chemical evidence of intake of sedative-hypnotics or aspiring in the blood and at least 2 blood samples (1 at lavage and 1 afterwards) were available for 62 participants (25 AC and 37 control participants)
	Inclusion criteria: taken a sedative-hypnotic or aspirin
	Degree of functional decompensation: moderate - slight impairment to unconscious, normal gag reflex and deep tendon reflexes, responsive to superficial pain; severe - unconscious with depressed or absent pain response, gag reflex and deep tendon reflexes to respiratory arrest
	Chemical proof of intake of sedative-hypnotics or aspirin
Interventions	*Intervention arm*:
	Type: gastric lavage + activated charcoal via nasogastric tube
	Timing: no information
	Dose: gastric lavage followed by 100 g AC
	Frequency: 1×
	Integrity: no information
	Control arm:

Comstock 1982 *(Continued)*

	Type: gastric lavage
	Timing: no information
	Dose: no information
	Frequency: 1×
	Integrity: no information
Outcomes	*Type (unit)*: percentage of participants showing increased blood drug concentrations (%) (data not extracted)
	Timing: blood samples were taken at the time of lavage and at 2 h to 4 h intervals thereafter when possible (early)
Funding	Supported by grant from the National Institute of Drug Abuse: grant 1 H81 DA 0175301
Notes	Of the initially 339 selected participants, only 62 had chemical proof of sedative-hypnotics or aspirin at at least 1 blood sample available, which constituted the study sample

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Following gastric lavage, 131 patients were randomly chosen to receive a slurry of 100 g of activated charcoal (Norit A) via the gastric tube." Comment: not enough information to make a judgment
Allocation concealment (selection bias)	Unclear risk	Quote: "Following gastric lavage, 131 patients were randomly chosen to receive a slurry of 100 g of activated charcoal (Norit A) via the gastric tube." Comment: not enough information to make a judgment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No information to support judgment, but lack of blinding is not likely to affect measurement of the outcomes studied
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Of the total population, 25 AC treated patients and 37 control patients had chemical evidence for the presence of one of the sedative-hypnotics listed in Tables la and lb or aspirin in the blood, and at least one blood sample in addition to the sample taken at lavage. These 62 patients constituted the population under study." Comment: only data from 62 out 339 randomized patients (18%) is presented. Loss to follow-up increases over time
Selective reporting (reporting bias)	High risk	Several clinically relevant outcomes (symptoms, adverse events) not reported
Other bias	High risk	Quote: "995 were ingestions by history and 339 or 34% were selected for gastric lavage at the discretion of the attending physician." Comment: potential bias during selection of the study population

Cooper 2005

Methods	*Study design*: randomized controlled trial
	Study duration: July 1999 to October 2000
	Setting: hospital (emergency department at tertiary referral teaching hospital, the Canberra Hospital)
	Country: Australia
	Number of individuals randomized: 327
	Number of individuals receiving the intervention: 166
	Number of individuals receiving the control: 161
	Number of individuals lost to follow-up: 0
	Sample size calculated: yes, a power of 80% to detect a 33% reduction in length of stay at the 5% level was anticipated
Participants	*Sex*:
	Control: 48 males and 113 females
	Intervention: 50 males and 116 females
	Age:
	Control: median age 28.5 years, IQR: 21.5-42.5 years
	Intervention: median age 31.5 years, IQR: 21-42 years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: participants presenting at the emergency department with a history of oral drug overdose. Benzodiazepines and paracetamol combined accounted for most of the overdoses (62-66%). 31-35% ingested more than one drug. Most subjects (57-59%) presented within 2 h after overdose. Glasgow Coma Scale was < 15 in 27-30% of cases.
	Inclusion criteria: ≥16 years, within 12 h following a deliberate oral overdose, thought to have ingested a substance adsorbed by AC
	Exclusion criteria (at discretion of treating physician): ingested a potentially toxic modified release preparation, presentation within 1 h of ingestion of a highly lethal substance (e.g. large doses of tricyclic antidepressants, antineoplastic medications, aspirin, cardioactive agents)
	Exclusion criteria: transferred, ingested substances not significantly adsorbed by AC (hydrocarbons, acids, alkalis), contraindications (unprotected airway, non-intact gastrointestinal tract)
Interventions	*Intervention arm*:
	Type: activated charcoal orally or via nasogastric tube + other treatment appropriate to the substances ingested
	Timing: after randomization
	Dose: 50 g (Norit-C) in 200 mL of water as slurry
	Frequency: 1×
	Integrity: 3 participants refused charcoal
	Control arm:

Type: no activated charcoal, only other treatment appropriate to the substances ingested

Timing: after randomization

Dose: NA

Frequency: NA

Integrity: 1 received charcoal

Outcomes	*Type (unit)*:
	Primary:
	Medical length of hospital stay (h) (see Table 4)
	Secondary:
	Requirement for ventilation
	Vomiting after admission
	Occurrence of aspiration
	Occurrence of death
	Timing: during hospital admission (intermediate)
Funding	The study was funded by the Australian Rotary Foundation and the Private Practice Trust Fund of The Canberra Hospital.
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomized to AC or no gastrointestinal decontamination, as indicated by the sealed sequentially numbered envelope contents." Comment: not enough information to make a judgment
Allocation concealment (selection bias)	Low risk	Quote: "Patients were randomized to AC or no gastrointestinal decontamination, as indicated by the sealed sequentially numbered envelope contents." Comment: adequate
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The treating medical staff were not blinded to the administration of AC, as this would be very difficult to achieve." Comment: not blinded, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "This decision was made by a senior member of the medical staff, but this was not usually a toxicologist or any other member of the study team... The coordinator and data manager of the study was never involved in the decision to medically discharge the patient." Comment: suggests that members of the study team are at least in some cases involved in outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Analysis was based on intention to treat..."

Cooper 2005 *(Continued)*

		Comment: analysis was appropriate, and there was very little deviation from protocol
Selective reporting (reporting bias)	Low risk	All relevant outcomes are reported
Other bias	Low risk	No other risk of bias detected

Crome 1983

Methods	*Study design*: randomized controlled trial
	Study duration: no information
	Setting: hospital: accident departments of multiple hospitals
	Country: UK
	Number of individuals randomized: 48
	Number of individuals receiving the intervention: 20
	Number of individuals receiving the control: 28
	Number of individuals lost to follow-up: 33
	Sample size calculated: no information
Participants	*Sex*: 10 males and 38 females
	Age:
	10-21 years: n = 7
	22-31 years: n = 12
	32-41 years: n = 8
	42-51 years: n = 7
	52-61 years: n = 4
	62-71 years: n = 2
	72-81 years: n = 1
	unknown: n = 7
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Presenting at the accident department with suspected overdose of tricyclic antidepressants and considered required to be hospitalized. Mixed dose were okay if tricyclic antidepressants were considered responsible for the symptoms.
	Of these 48 cases, 17 had taken tricyclic antidepressants alone, 13 in combination with other drugs, 7 had not taken antidepressants and 11 did not have significant amounts of any drug in their blood
	Inclusion criteria: symptoms considered to be caused by tricyclic antidepressants, patient will be admitted to hospital

Crome 1983 *(Continued)*

Interventions	*Intervention arm*:
	Type: activated charcoal in water suspended (+ supportive care), given through a nasogastric tube after gastric lavage in obtunded patients and as a drink in conscious and co-operative patients
	Timing: no information
	Dose: 10 g in 200 mL water
	Frequency: 1×
	Integrity: no information
	Control arm: supportive care, which might include gastric lavage, otherwise not specified
	Type: NA
	Timing: NA
	Dose: NA
	Frequency: NA
	Integrity: NA
Outcomes	*Type (unit)*:
	Grade of coma
	Presence of convulsions/movement disorders
	Presence of pyramidal signs
	Anticholinergic signs
	Airway inserted, intubated and/or ventilated
	Heart rate, rhythm, ECG
	Blood pressure
	Respiratory rate
	Timing:
	Clinical information was recorded on admission and at 4 h, 8 h and 24 h and at discharge (intermediate)
	Blood samples were collected on admission and at 4, 8 and 24 h (intermediate)
	Urine and gastric washings were collected.
Funding	Grant from Leo Research Foundation pharmaceutical company
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Local randomisation by sealed envelopes" (personal communication)
		Comment: not enough information to make a judgment

Crome 1983 (Continued)

Allocation concealment (selection bias)	Unclear risk	Quote: "Local randomisation by sealed envelopes" (personal communication) Comment: sealed envelopes were kept in emergency departments of participating hospitals, but not specified whether these were opaque and sequentially opened
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Were outcome assessors blinded? No" (personal communication) Comment: lack of blinding might affect measurement of the outcomes at study
Incomplete outcome data (attrition bias) All outcomes	High risk	For the main outcome reported, coma, only data for pure tricyclic antidepressant were reported and not for the other subgroups. Although 17 participants are reported to make up this subgroup, data for 15 participants is reported. Participants that refused to ingest AC were not included in the analysis, no intention-to-treat analysis (personal communication)
Selective reporting (reporting bias)	High risk	Pre-specified outcomes presence of convulsions/movement disorders, presence of pyramidal signs, anticholinergic signs, airway inserted, intubated and/or ventilated, heart rate, heart rhythm, ECG, blood pressure and respiratory rate were not reported
Other bias	High risk	In 11 of the 48 participants no significant amounts of any drugs were found and 7 of them had not taken any tricyclic antidepressant Role of the study funder not clarified

De Silva 2003

Methods	*Study design*: randomized controlled trial *Study duration*: November 2001 to June 2002 *Setting*: hospital setting (accident and emergency department of the Kurunegala Teaching Hospital) *Country*: Sri Lanka *Number of individuals randomized*: 401 *Number of individuals receiving the intervention*: 201 *Number of individuals receiving the control*: 200 *Number of individuals lost to follow-up*: 23 *Sample size calculated*: yes, a sample size of 376 was calculated to detect a decrease in death rate from 10% to 2.5% with 80% power at the 5% level
Participants	*Sex*: SDAC: 111 males and 89 females MDAC: 87 males and 114 females *Age*:

De Silva 2003 *(Continued)*

SDAC: 24.1 (SD 8.7) years

MDAC: 23.5 (SD 9.6) years

Country (if different from study authors'): NA

Type, dose and timing of poisoning: yellow oleander seed poisoning, presenting within 24 h of ingestion

Inclusion criteria: yellow oleander tree poisoning; 12-70 years old; presenting within 24 h of poisoning

Exclusion criteria: taken another drug (e.g. alcohol, organophosphates, paracetamol, or sedatives); debilitating disease (diabetes mellitus, hepatic or renal disease, heart failure, or malignant disease); abdominal surgery within the past year; known hypersensitivity to AC; severe infection; pregnant and lactating women

Interventions	*Intervention arm*:
	Type: MDAC and supportive care (which included gastric lavage, followed by a first dose of AC, atropine and metoclopramide as required)
	Timing: initial dose on admission, after gastric lavage, additional doses every 6 h for 3 days: 0 h, 6 h, 12 h, 18 h, 24 h, 30 h, 36 h, 42 h, 48 h, 54 h, 60 h, 66 h, 72 h
	Dose: 50 g in 400 mL water
	Frequency: 13×
	Integrity: 16 discharged themselves before end of treatment. Although most participants found the charcoal unpalatable, none refused to take it.
	Control arm:
	Type: SDAC + water and supportive care (which included gastric lavage, atropine and metoclopramide as required)
	Timing: on admission, after gastric lavage
	Dose: 50 g dose AC + 400 mL, followed by 400 mL water every 6 h as placebo
	Frequency: 1×
	Integrity: 10 discharged themselves before end of treatment

Outcomes	*Type (unit)*:
	Primary outcome:
	Death
	Secondary outcomes:
	ICU admission
	Participants given anti-digoxin antibody Fab fragments
	Cardiac pacing
	Life-threatening arrhythmias at 24 h
	Atropine administered (mg)
	Boluses of atropine administered
	Time in hospital (days) (see Table 4)
	Patient response to treatment

De Silva 2003 *(Continued)*

	Bowel sounds
	Timing: data collected until death or discharge from hospital (intermediate)
Funding	The University of Kelaniya gave financial support for the study.
Notes	Sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors declared no conflict of interest
	23/26 participants that left the hospital before end of treatment were confirmed to be alive and well within 1 week of leaving the hospital. 3 that could not be contacted were considered and analysed as being alive.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "6 h after admission, an investigator (AP) used a computer-generated random-allocation table to allocate patients ... This investigator was not involved in care or assessment of patients." Comment: adequate
Allocation concealment (selection bias)	Low risk	Quote: "6 h after admission, an investigator (AP) used a computer-generated random-allocation table to allocate patients ... This investigator was not involved in care or assessment of patients." Comment: adequate
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Investigators were unaware of patients' treatment allocation. Three medically qualified research assistants supervised administration of activated charcoal or sterile water, but they did not participate in clinical assessment or management of patients. To facilitate blinding, research assistants also ensured that patients and their bedclothes were cleaned thoroughly after each treatment." Comment: participants were not blinded, but lack of blinding is not likely to affect the outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Investigators were unaware of patients' treatment allocation. Three medically qualified research assistants supervised administration of activated charcoal or sterile water, but they did not participate in clinical assessment or management of patients. To facilitate blinding, research assistants also ensured that patients and their bedclothes were cleaned thoroughly after each treatment." Comment: adequate, outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Analysis was by intention to treat.", "26 (16 in the treatment group) patients discharged themselves within 72 h of admission; all had normal heart rates at the time they left hospital, and 23 (16 in the treatment group) reported being well when contacted at their homes within 1 week" Comment: low attrition rate (6%), which was accounted for and analysed as intention-to-treat
Selective reporting (reporting bias)	High risk	Quote: "The most frequent adverse effects of treatment with multiple doses of activated charcoal were diarrhoea and abdominal discomfort. Three patients had diarrhoea and 13 complained of abdominal discomfort."

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De Silva 2003 *(Continued)*

		Comment: potential adverse events not clearly described for the control group and for the outcome 'boluses of atropine administered' statistical analyses and reported summary effect were not clear
Other bias	Low risk	No other risk of bias detected

Eddleston 2008

Methods	*Study design*: randomized controlled trial
	Study duration:
	Total: 31 March 2002 to September 2004
	Anuradhapura: 31 March 2002 to September 2004
	Polonnaruwa: 4 June 2002 to September 2004
	Kurunegala: 23 November 2002 to 3 Febrary 2003
	Setting: hospital setting (medical wards of 3 Sri Lankan secondary hospitals)
	Country: UK
	Number of individuals randomized: 4632
	Number of individuals receiving the intervention:
	SDAC: 1545
	MDAC: 1533
	Number of individuals receiving the control: 1554
	Number of individuals lost to follow-up: 3
	Sample size calculated: yes, a total sample size of 4200 was calculated to measure a decrease in mortality from 10% to 7%, with 80% power at the 5% level
Participants	*Sex*:
	No AC: 915 men and 639 women
	SDAC: 883 men and 662 women
	MDAC: 960 men and 573 women
	Age:
	No AC: 25 (19-35)
	SDAC: 25 (19-35)
	MDAC: 25 (19-36)
	Country (if different from study authors'): Sri Lanka
	Type, dose and timing of poisoning: participants admitted to the medical ward of 3 secondary referral hospitals with a history of oral poisoning
	Median time between ingestion and admission (h, mean (IQR))
	Usual care: 4.2 (2.7 to 7.0)

Eddleston 2008 *(Continued)*

SDAC: 4.2 (2.7 to 7.1)

MDAC: 4.3 (2.7 to 7.1)

Type of poisoning:

Usual care:

Oleander: 555

Organophosphorus/carbamate pesticide: 441

Organochlorine: 4

Other/unknown pesticide or paraquat: 343

Medicine or unknown: 211

SDAC:

Oleander: 550

Organophosphorus/carbamate pesticide: 440

Organochlorine: 3

Other/unknown pesticide or paraquat: 340

Medicine or unknown: 212

MDAC:

Oleander: 542

Organophosphorus/carbamate pesticide: 429

Organochlorine: 3

Other/unknown pesticide or paraquat: 345

Medicine or unknown: 214

Participants were stabilized upon admission by resuscitation, by airway stabilization and providing oxygen, atropine, fluid and antidotes, as necessary, before intervention started

Exclusion criteria: < 14 years, prior treatment with AC during this episode of poisoning, known pregnancy, ingestion of corrosives or hydrocarbons alone, requirement for oral medication, inability to intubate the patient with a Glasgow coma score < 13, presentation > 72 h after ingestion, previous recruitment, < 16 years old or unconscious without relatives present to give consent

Interventions	*Intervention arm*:

Type: SDAC or MDAC orally or via nasogastric tube + supportive care (see control)

Timing:

SDAC: "soon" after admission

MDAC: every 4 h

Dose: 50 g superactivated charcoal (Carbomix) in 300 mL water per dose

Frequency:

SDAC: 1×

MDAC: 6×

Eddleston 2008 *(Continued)*

Integrity: first protocol intended to deliver 18 doses of AC in the multi-dose group, this however was not feasible, so protocol was adapted to 6 doses. Compliance was not anticipated a problem as was given while patient was under supervision; however participants were not forced. An analysis of compliance was done in 2 of the 3 hospitals, involving 1103 participants, showing that compliance decreased to 66% by the 6th dose of AC. Furthermore, an estimated 8% of the first dose of AC was vomited. This amount decreased to 1% by the sixth dose. < 5% did not receive allocated intervention (reasons included damaged throat and refusal)

Control arm:

Type: supportive care: resuscitated if needed, stabilized and given oxygen and antidotes as necessary. Atropine (usually 0.3–0.6 mg/h) and intravenous fluids were administered as needed to maintain a heart rate > 70 bpm and systolic blood pressure > 80 mm Hg. Participants with severe cardiotoxicity either were administered antidigoxin Fab antitoxin or treated with temporary pacing. Most participants, 54% and 7.5% respectively, received forced emesis or gastric lavage prior to arriving at the study hospital.

Initially gastric lavage was never performed at study hospital. However, after patient 1905, in participants presenting less than 2 h with significant poisonings gastric lavage was performed (3 × 300 mL)

Timing: NA

Dose: NA

Frequency: NA

Integrity: NA

Outcomes	*Type (unit)*: Primary outcome: All-cause mortality Secondary outcomes (per ingested poison): For organophosphorus or carbamate pesticide: Intubation Time ventilated Time to first ventilation Seizures For oleander poisoning: Cardiac dysrhythmias needing digoxin-specific antibody fragments, serum potassium > 6.0 mmol/L or temporary pacing *Timing*: participants were seen at least every 3 h and more if needed. Condition of participants was recorded twice per day at 8:30 and 20:30. Significant events (intubation, seizures, death) were recorded at time of the event (intermediate)
Funding	Grant 063560 from the Wellcome Trust's Tropical Interest Group to ME. The South Asian Clinical Toxicology Research Collaboration is funded by a Wellcome Trust/National Health and Medical Research Council International Collaborative Research Grant 071669.
Notes	The funding source had no role in study design, data collection, data analysis, and data interpretation; or writing of the report; or in the decision to submit for publication. The authors declared no conflict of interest. Trial registration number: ISRCTN02920054

Eddleston 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The random allocation sequence was generated by computer and incorporated into a Microsoft Access programme written for patient recruitment, randomisation and event recording (Figure 1). Stratified block randomisation was performed using the following strata:" Comment: adequate
Allocation concealment (selection bias)	Low risk	Quote: "The allocation sequences were generated independently by the study statistician (EJ) and implemented by the programmer (SA), neither of whom had a role in patient recruitment, treatment or assessment. Variable block sizes of 3, 6 and 9 were used to allocate patients in equal numbers to each treatment group... Randomisation occurred after the patient's baseline data had been entered and receipt of consent noted, and could not be manipulated by study doctors. The recruiting doctor was unable to predict allocation before randomisation." Comment: adequate
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Another limitation was the absence of masking. We believed that masking was difficult because of the impossibility to conceal from a reviewing doctor whether a patient had received any charcoal. An absence of masking might have allowed for performance bias for the secondary outcomes. To counter this potential bias, the medical team made decisions about intubation and transfer of patients independently of the study doctors." Comment: participants and personnel were not blinded, which may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Another limitation was the absence of masking. We believed that masking was difficult because of the impossibility to conceal from a reviewing doctor whether a patient had received any charcoal. An absence of masking might have allowed for performance bias for the secondary outcomes. To counter this potential bias, the medical team made decisions about intubation and transfer of patients independently of the study doctors." Comment: outcome assessors were not blinded, but primary outcome was unambiguous
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "We did an intention-to-treat analysis on all patients with available outcomes data (loss to follow-up of three (< 1%) patients) analysed in the groups to which they were allocated." Comment: adequate
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes have been reported
Other bias	Low risk	No other risk of bias detected

Hultén 1988

Methods	*Study design*: randomized controlled trial
	Study duration: no information

Hultén 1988 *(Continued)*

	Setting: hospital setting
	Country: Sweden
	Number of individuals randomized: 91
	Number of individuals receiving the intervention: 34
	Number of individuals receiving the control: 43
	Number of individuals lost to follow-up: 14
	Sample size calculated: no information
Participants	*Sex*: no information
	Age: older than 14 years
	Country (if different from study authors'): UK, Belgium, Sweden
	Type, dose and timing of poisoning: 32 participants took amitriptyline, 16 clomipramine, 10 mianserin, 9 imipramine, 6 dothiepin, 2 doxepin, 2 nortriptyline, mixed overdoses in 67% with most commonly benzodiazepines or alcohol
	Inclusion criteria: participants with self-poisoning with 1 or more of 7 different TCA (mixed overdoses also included if clinician considered 1 of 7 TCA drugs was major cause of participants' symptoms)
	Exclusion criteria: participants < 14 years old, taken significant amount of other drugs
	Plasma TCA concentration < 0.3 µg/L
Interventions	*Intervention arm*:
	Type: activated charcoal (Medicoal[R]) after gastric lavage
	Timing: no information
	Dose: 20 g
	Frequency: 1×
	Integrity: no information
	Control arm:
	Type: gastric lavage
	Timing: no information
	Dose: no information
	Frequency: 1×
	Integrity: no information
Outcomes	*Type (unit)*:
	AUC ((mg/L) × h)
	Blood pressure (mmHg)
	Heart rate (bpm)
	Coma grade (Matthew-Lawson coma scale)
	Symptoms: e.g. convulsions, arrhythmias, muscle twitching

Hultén 1988 *(Continued)*

Number of participants intubated

Time spent intubated

Time admitted to ICU (see Table 4)

Time admitted to hospital (see Table 4)

Timing:

Plasma drug concentration at 0 h, 1 h, 2 h, 4 h, 8 h and 24 h (intermediate)

Blood pressure, heart rate, coma grade and symptoms at 0 h, 4 h, 8 h and 24 h (intermediate)

Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed by using rand numbers and equilibration made by groups of 10." Comment: adequate randomization
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization was performed by using rand numbers and equilibration made by groups of 10." Comment: not enough information to make a judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "14 patients were excluded because they had taken a significant amount of other drugs" Comment: adequate explanation
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes have been reported
Other bias	Low risk	No other risk of bias detected

Ilett 1977

Methods	*Study design*: randomized controlled trial
	Study duration: no information
	Setting: hospital setting (emergency centre at Royal Perth Hospital)

Country: Australia

Number of individuals randomized: 120

Number of individuals receiving the intervention:

USP 15 mL: 38

APF 15 mL: 34

Number of individuals receiving the control:

APF 30 mL: 33

Number of individuals lost to follow-up: 15

Sample size calculated: no information

Participants	*Sex*: 100 females, 20 males
	Age:
	Females: 27 (SD 10) years
	Males: 29 (SD 8.9) years
	Range: 13-64 years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: benzodiazepine tranquillizers or hypnotics (n = 37), other tranquillizers (n = 4), other hypnotics (n = 18), antidepressants (n = 7), analgesics (n = 30), antihistamines (n = 3), miscellaneous drugs and chemicals (n = 26)
	Exclusion criteria: only partial dose was taken (n = 2), left monitored field (n = 2), physician in charge ordered alternative treatment because of deterioration of patient's condition, insufficient data collected
Interventions	*Intervention arm 1*:
	Type: syrup of ipecacuanha formulated according to the American Pharmacopeia (USP), 0.12% w/v alkaloid content.
	Timing: upon admission
	Dose: 15 mL followed by 200 mL of water
	Frequency: 1×, participants who did not vomit within 30 minutes of the first dose were given a second identical dose and an additional 200 mL of water
	Integrity: no information
	Intervention arm 2:
	Type: syrup of ipecacuanha formulated according to the Australian Pharmaceutical Formulary (APF) 0.14 w/v alkaloid content.
	Timing: upon admission
	Dose: 15 mL followed by 200 mL of water
	Frequency: 1×, participants who did not vomit within 30 minutes of the first dose were given a second identical dose and an additional 200 mL of water.
	Integrity: no information
	Intervention arm 3:

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Ilett 1977 *(Continued)*

Type: syrup of ipecacuanha APF

Timing: upon admission

Dose: 30 mL followed by 200 mL of water

Frequency: 1×, participants who did not vomit within 30 minutes of the first dose were given a second identical dose and an additional 200 mL of water

Integrity: no information

Outcomes	*Type (unit)*:
	Incidence of vomiting (data not extracted)
	Time to vomit (min) (data not extracted)
	Number of times vomiting occurred (data not extracted)
	Volume of vomitus (mL) (data not extracted)
	Timing: on occurrence (no information)
Funding	No information
Notes	Data for syrup of ipecacuanha USP vs syrup of ipecacuanha APF not extracted, because not within scope of this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were allocated sequentially to the treatments, which had been previously randomized by means of a table of random numbers". Comment: adequate
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were allocated sequentially to the treatments, which had been previously randomized by means of a table of random numbers". Comment: not enough information to make a judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The trial was conducted at a double blind design" Comment: not enough information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The trial was conducted at a double blind design" Comment: not enough information to support judgment, but lack of blinding may affect outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Low risk	15/120 (12.5%) is lost to follow-up: 2 only took partial dose, 2 left monitored field, 6 received alternative treatment because of deterioration of condition, 5 with insufficient data. Not a high attrition rate, adequately explained
Selective reporting (reporting bias)	High risk	No reporting of potential adverse events. No data on symptom severity or drug absorption/dug recovery
Other bias	Low risk	No other risk of bias detected

James 1995

Methods	*Study design*: randomized controlled trial
	Study duration: February 1993 to January 1994
	Setting: hospital setting (emergency department)
	Country: USA
	Number of individuals randomized: 119
	Number of individuals receiving the intervention:
	Sorbitol: 32
	Magnesium citrate: 33
	Magnesium sulphate: 23
	Number of individuals receiving the control: 28
	Number of individuals lost to follow-up:3
	Sample size calculated: sample size calculations determined that a minimum of 25 participants were needed in each treatment group to detect a difference in mean time to the first stool of 4 h, using a power of 0.80 and an α of 0.10
Participants	*Sex*: no information
	Age: 25 (SD 8) months, range 1-5 years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: variety of toxins (analgesics, anticonvulsants, antihistamines and decongestants, asthma therapies, automotive products, cardiovascular drugs, gastrointestinal preparations, insecticides, mushrooms, psychotropic drugs, rodenticides, topicals, miscellaneous drugs)
	Inclusion criteria: suspected acute ingestions in which activated charcoal and a cathartic were indicated. Parents of participants had to have telephone access for follow-up purposes.
Interventions	*Intervention arm 1*:
	Type: sorbitol
	All treatments were administered as a slurry with 1 g/kg activated charcoal. Participants also received syrup of ipecac or gastric lavage.
	Timing: as soon as possible
	Dose: 50% solution, 2 g/kg. Administered as a slurry with 1 g/kg activated charcoal per nasogastric tube.
	Frequency: 1×, if emesis occurred after administration of the cathartic/charcoal slurry, additional doses were administered at the discretion of the attending physician in the emergency department
	Integrity: no information
	Intervention arm 2:
	Type: magnesium citrate
	All treatments were administered as a slurry with 1 g/kg activated charcoal. Participants also received syrup of ipecac or gastric lavage

James 1995 *(Continued)*

Timing: as soon as possible

Dose: 233 mg/kg. Administered as a slurry with 1 g/kg activated charcoal per nasogastric tube.

Frequency: 1×, if emesis occurred after administration of the cathartic/charcoal slurry, additional doses were administered at the discretion of the attending physician in the emergency department

Integrity: no information

Intervention arm 3:

Type: magnesium sulphate

All treatments were administered as a slurry with 1 g/kg activated charcoal. Participants also received syrup of ipecac or gastric lavage

Timing: as soon as possible

Dose: 6.25% solution, 250 mg/kg. Administered as a slurry with 1 g/kg activated charcoal per nasogastric tube

Frequency: 1×, if emesis occurred after administration of the cathartic/charcoal slurry, additional doses were administered at the discretion of the attending physician in the emergency department

Integrity: no information

Control arm:

Type: water

Timing: as soon as possible

Dose: no information

Frequency: 1×

Integrity: no information

Outcomes	*Type (unit)*:
	Mean time to stool (h) (data not extracted)
	Number of stools during 24 h (data not extracted)
	Occurrence of side effects
	Timing:
	Telephone follow-ups at 1 h, 4 h, 8 h and 24 h after completion of cathartic administration (intermediate).
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not enough information to make a judgement
Allocation concealment (selection bias)	Unclear risk	Not enough information to make a judgement

James 1995 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Physicians, nurses and parents were blinded. Cathartics were formulated for delivery at a uniform volume in opaque bottles." Comment: adequate
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Poison control centre staff who conducted telephone follow-ups were blinded" Comment: adequate
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 participants were lost to follow-up, and not included in the analysis. Low attrition rate: 2.5%
Selective reporting (reporting bias)	High risk	Important outcomes, clinical outcomes, are not measured
Other bias	Low risk	No other risk of bias detected

Kornberg 1991

Methods	*Study design*: randomized controlled trial
	Study duration: 2 years (November 1987 to November 1989)
	Setting: hospital setting (pediatric emergency department of the Children's Hospital of Buffalo)
	Country: USA
	Number of individuals randomized: 70
	Number of individuals receiving the intervention: 32
	Number of individuals receiving the control: 38
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: SOI: 39 boys, 31 girls; AC: 17 boys and 15 girls
	AC: 22 boys and 16 girls
	Age:
	SOI and AC group: 2.5 (SD 0.2) years
	AC alone group: 2.3 (SD 0.2) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: wide variety of ingested substances, most common was acetaminophen
	Inclusion criteria: orally poisoned participants less than 6 years old presenting to the ED
	Exclusion criteria: not awake or without a definite gag reflex, deteriorating level of consciousness, vomited or received SOI before ED arrival, or ingested hydrocarbons, corrosives, iron, ethanol alone or acetaminophen alone if more than 6 h before ED arrival
Interventions	*Intervention arm*:

Kornberg 1991 *(Continued)*

Type: SOI + 160 mL tap water or apple juice + activated charcoal (Actidose) with sorbitol

Timing: SOI: on admission, AC after vomiting occurred (mean time 2.1 h after SOI)

Dose: SOI: 15 mL, AC: 1 g/kg premixed with 40% sorbitol

Frequency: 1× but repeated if no emesis occurred after 30 min

Integrity: no information.

Control arm:

Type: activated charcoal (Actidose) with sorbitol

Timing: on admission

Dose: 1 g/kg with 40% sorbitol

Frequency: 1×

Integrity: AC was presented orally, but if patient was unwilling or unable to take AC orally, it was given by nasogastric tube

Outcomes	*Type (unit)*:
	Time to ED (h) (see Table 4)
	Time in ED (h) (see Table 4)
	Time to receive AC (h)
	Hospital admission
	Improved in ED
	Emesis of AC
	Time in ED (if discharged) (h) (see Table 4)
	Timing:
	On occurrence (early)
Funding	Study was not funded (personal communication)
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera-tion (selection bias)	High risk	Quote: "They were randomized into two groups based on the date of arrival." Comment: randomization based on even/odd days
Allocation concealment (selection bias)	High risk	Quote: "They were randomized into two groups based on the date of arrival." Comment: allocation based on the date of arrival does not allow for adequate allocation concealment
Blinding of participants and personnel (perfor-mance bias) All outcomes	High risk	No blinding (personal communication), which might affect the subjective out-comes admission to ED, improvement in ED, time to discharge from ED

Kornberg 1991 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding (personal communication), which might affect subjective outcome measures, such as admission to ED, improvement in ED, time to discharge from ED
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported, all subjects included in analysis
Selective reporting (reporting bias)	Low risk	No reason to believe there is reporting bias
Other bias	Low risk	No other risk of bias detected

Kulig 1985

Methods	*Study design*: randomized controlled trial
	Study duration: 18 months (June 1981 to December 1982)
	Setting: hospital setting (emergency department of Denver General Hospital)
	Country: USA
	Number of individuals randomized: 630
	Number of individuals receiving the intervention:
	214 ipecac + AC
	72 gastric lavage + AC (data not extracted)
	Number of individuals receiving the control:
	262 AC orally
	44 AC via nasogastric tube (data not extracted)
	Number of individuals lost to follow-up: 38
	Sample size calculated: no information
Participants	*Sex*: 268 male and 324 female (based on 592 finally included participants)
	Age: 29.3 (8 months to 80 years) (based on 592 finally included participants)
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: any kind over oral drug overdose not mentioned in exclusion criteria
	Exclusion criteria: emesis occurred spontaneously or after administration of activated charcoal; ipecac had been administered prior to arrival; ingested poison was a hydrocarbon, corrosive, iron, strychnine or if acetaminophen was ingested alone; ethanol alone had been ingested
Interventions	*Intervention arm*:
	Type: syrup of ipecac + activated charcoal-magnesium sulphate, in addition to vigorous supportive care if needed (including airway support, ventilation, antidotes, anticonvulsants, antiarrhythmic and pressors)
	Timing: on admission

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Kulig 1985 *(Continued)*

Dose:

SOI: no information

AC-magnesium sulphate: 30-50 g AC mixed with 20 g magnesium sulphate (250 mg/kg for a child) and water

Frequency: 1×

Integrity: no information

Control arm:

Type: activated charcoal + magnesium sulphate, in addition to vigorous supportive care if needed (including airway support, ventilation, antidotes, anticonvulsants, antiarrhythmic and pressors)

Timing: on admission

Dose: 30-50 g mixed into a slurry with 20 g $MgSO_4$ (or 250 mg/kg for a child)
Frequency: 1×

Integrity: no information

Outcomes	*Type (unit)*:
	Number of admissions
	Clinical deterioration
	Clinical improvement
	Mortality
	Timing: on occurrence: ED data were collected on a standard toxicology form created for the study, which detailed the patient's history, physical examination, laboratory data, and clinical course (early)
Funding	McNeil Consumer Products Company
Notes	Data for gastric lavage vs AC administered via nasogastric tube were not extracted, because not within scope of this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients arriving on odd-numbered days were treated in the traditional manner by receiving syrup of ipecac. Patients presenting on even-numbered days did not undergo gastric emptying procedures, but only received activated charcoal and the cathartic." Comment: no adequate randomization
Allocation concealment (selection bias)	High risk	Quote: "Patients arriving on odd-numbered days were treated in the traditional manner by receiving syrup of ipecac. Patients presenting on even-numbered days did not undergo gastric emptying procedures, but only received activated charcoal and the cathartic." Comment: randomization process allows to know in which group the next participants will be allocated
Blinding of participants and personnel (performance bias)	Unclear risk	No information on blinding, but not possible due to nature of interventions. May affect outcomes studied

Kulig 1985 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Low risk	38 participants were excluded because they were not treated according to protocol. Low attrition rate: 38/630 = 6%
Selective reporting (reporting bias)	High risk	No reporting of adverse data such as nausea. Sample sizes of subgroups not reported
Other bias	Low risk	No other risk of bias detected

Merigian 1990

Methods	*Study design*: randomized controlled trial
	Study duration: October 1986 to March 1988
	Setting: hospital setting
	Country: USA
	Number of individuals randomized:820
	Number of individuals receiving the intervention:
	asymptomatic: 220
	symptomatic: 163 (data not extracted)
	Number of individuals receiving the control:
	asymptomatic: 231
	symptomatic: 194 (data not extracted)
	Number of individuals lost to follow-up: 5
	Sample size calculated: no information
Participants	*Sex*: no significant difference in male/female ratio between AC and control group
	Age: no significant difference in age between AC and control group
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: self-reported poisoning with substances other than described in exclusion criteria.
	Selection criteria: excluded if their presenting history included ingestion of any of the following: acetaminophen > 140 mg/kg, lithium, monoamine oxidase inhibitors, heavy metals, formaldehyde, mushrooms, digitalis, methanol, ethylene glycol, iron, or sustained release products. Diagnostic criteria: AMSE score ≥ 7, GCS of 15 and vital signs in the following ranges: systolic blood pressure between 110 mm Hg and 160 mm Hg, diastolic blood pressure between 60 mm Hg and 100 mm Hg, pulse rate between 60 beats/min and 110 beats/min, temperature between 36.4°C and 37.5°C (oral)
Interventions	*Intervention arm*:

Merigian 1990 *(Continued)*

Type: oral activated charcoal

Timing: no information

Dose: 50 g

Frequency: 1×

Integrity: no information

Control arm:

Type: observation only

Timing: NA

Dose: NA

Frequency: NA

Integrity: NA

Outcomes	*Type (unit)*:
	Clinical deterioration
	Time in ED (min) (see Table 4)
	Admission to ICU
	Intubation
	Duration of intubation (h)
	Timing: each patient was observed for 4 h (early)
Funding	No information
Notes	Data for asymptomatic participants (receiving ipecac or gastric lavage) were not extracted, because these were analyzed as one group (gastric emptying)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients presenting with asymptomatic overdoses were given 50 grams of AC orally on even days and were simply observed without AC on odd days." Comment: alternation is not an adequate randomization method
Allocation concealment (selection bias)	High risk	Quote: "Patients presenting with asymptomatic overdoses were given 50 grams of AC orally on even days and were simply observed without AC on odd days." Comment: does not allow for allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied

Merigian 1990 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Low risk	No unexplained loss to follow-up. Only small number of participants (5/451 = 1.1%) excluded from analysis due to receiving incorrect treatment
Selective reporting (reporting bias)	Low risk	No reason to believe there is reporting bias
Other bias	High risk	Study only observes the effects of AC in asymptomatic participants, which are more likely not to experience a benefit from a treatment

Merigian 2002

Methods	*Study design*: randomized controlled trial
	Study duration: inclusion period was 24 months, 1992-1994, no follow-up after hospital discharge
	Setting: hospital setting: emergency department of a regional medical center
	Country: USA
	Number of individuals randomized: 1479
	Number of individuals receiving the intervention: 404
	Number of individuals receiving the control: 1075
	Number of individuals lost to follow-up: 1
	Sample size calculated: no information
Participants	*Sex*: 688 males and 791 females
	Age: 30 (SD 10.4) years (range 22-82 years)
	Country (if different from study authors'): USA (61% African-American, 38% white, < 1% other)
	Type, dose and timing of poisoning:
	Participants with a history of recent oral drug overdose. Not specified further. 48% reported ingesting a single agent, 52% ingested 2 or more drugs
	Exclusion criteria: more than 140 mg/kg paracetamol ingested; inhalation/ingestion of crack; ingestion of mushrooms, volatiles, caustic agents, heavy metals, lithium, iron preparations; participants did not receive a gastric emptying or lavage procedure
Interventions	*Intervention arm*:
	Type: oral activated charcoal + supportive therapy when necessary (including but not limited to: maintenance of airway, pulmonary hygiene, intubation, circulatory support, assurance of adequate urine output and renal function)
	Timing: no information
	Dose: 50 g
	Frequency: 1×

Merigian 2002 *(Continued)*

Integrity: 1 patient was excluded from the analysis due to receiving lavage at the emergency department. 4 others received lavage but stayed in the study, 3 in the ICU and one before being transferred to the hospital.

Control arm:

Type: supportive therapy (including but not limited to: maintenance of airway, pulmonary hygiene, intubation, circulatory support, assurance of adequate urine output and renal function)

Timing: NA

Dose: NA

Frequency: NA

Integrity: NA

Outcomes	*Type (unit)*:
	Length of stay in the emergency department (ED) (h) (see Table 4)
	Length of stay in the intensive care unit (ICU) (h) (see Table 4)
	Clinical deterioration of symptoms (defined by presence of one of pre-defined parameters: table 1)
	Proportion of intubation
	Duration of intubation (h)
	Adverse events/complications
	Incidence of vomiting
	Timing: on occurrence or at discharge (intermediate)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Our protocol required that patients given OAC be observed in the ED for a minimum of 4 hours on even days. On odd days, patients received supportive observation only, with no OAC administration, for a minimum of 4 hours." Comment: alternation is not an adequate randomization method
Allocation concealment (selection bias)	High risk	Quote: "Our protocol required that patients given OAC be observed in the ED for a minimum of 4 hours on even days. On odd days, patients received supportive observation only, with no OAC administration, for a minimum of 4 hours." Comment: randomization process does not allow for allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither participants nor personnel were blinded, which may affect outcomes studied

Merigian 2002 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding of outcome assessors; could influence subjective outcomes studied
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 patient was excluded from the analysis due to receiving lavage at the emergency department. 4 others received lavage but stayed in the study, 3 in the ICU and one before being transferred to the hospital. All received activated charcoal. Low attrition rate: 1/404 (0.25%)
Selective reporting (reporting bias)	High risk	No reporting of the amount of intubations in the ED or hospital groups, no reporting of the time of intubation in the ICU group, selectively grouping of the ED and hospital groups for the outcome time of intubation
Other bias	High risk	Post hoc analyses according to clinical severity
		No follow-up after discharge from the hospital

Montoya-Cabrera 1999

Methods	*Study design*: randomized controlled trial
	Study duration: blood sampling was done up to 48 h, mean duration between final and initial dose of treatment was 21 h (range 6-36 h)
	Setting: hospital setting: toxicology department of a children's hospital
	Country: Mexico
	Number of individuals randomized: 14
	Number of individuals receiving the intervention: 7
	Number of individuals receiving the control: 7
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: no information, but from both sexes.
	Age: mean: 2 years and 5 months (range 8 months to 8 years and 2 months)
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: children admitted to the toxicology department with suspected overdose of paracetamol of 122 (SD 81) mg/kg (54-247 mg/kg), with a delay of 60 h (10-168 h)
	Inclusion criteria: overdose was defined as an administered dose that was higher than therapeutic (10-15 mg/kg) and plasma levels of paracetamol were over 20 mg/mL for over 4 h
Interventions	*Intervention arm*:
	Type: N-acetylcysteine, as in the control group, followed by AC (with magnesium sulphate), also delivered via the nasogastric tube
	Timing:
	AC: every 4 h for 24 h
	$MgSO_4$: every 12 h

Montoya-Cabrera 1999 *(Continued)*

Dose:

1 g/kg AC, suspended in 120-200 mL saline

1 g/kg $MgSO_4$, added to the AC

Frequency: 6× AC

Integrity: no information

Control arm:

Type: N-acetylcysteine, administered via a nasogastric tube

Timing: upon admission and every 4 h

Dose: initial dose of 140 mg/kg, followed by repeat doses of 70 mg/kg

Frequency: 18×

Integrity: no information

Outcomes	*Type (unit)*:
	Elimination half-life: $T_{1/2}$ (h)
	Total body clearance Cl_B (mL × kg × min)
	Prothrombin time
	Aminotransferases ASAT & ALAT (U/dL) (data not extracted)
	Timing: blood was sampled at 0 h, 24 h and 48 h (intermediate)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on how randomization was achieved
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No information on blinding, but should not affect outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No indication of incomplete outcomes.

Montoya-Cabrera 1999 *(Continued)*

Selective reporting (reporting bias)	High risk	No standard deviations for main outcomes of interest, no information about clinical course of the overdose, especially with regard to the obvious and not further investigated difference in hepatic toxicity between groups
Other bias	High risk	Hepatic toxicity marker values suggest a clinically meaningful difference between the 2 treatment groups

Passeron 1989

Methods	*Study design*: randomized controlled trial
	Study duration: no information on recruitment period, delay before presentation to the hospital was comparable between groups mean: intervention: 6.2 (SD 4.6); control: 7 (SD 4.6). Clinical follow-up was done up to 48 h after administration/no administration of AC.
	Setting: hospital setting: emergency department of a university hospital
	Country: France
	Number of individuals randomized: 32
	Number of individuals receiving the intervention: 16
	Number of individuals receiving the control: 16
	Number of individuals lost to follow-up: 7 (44%) and 2 (13%) participants in control and intervention group did not have a blood sample at 9 h
	Sample size calculated: no information
Participants	*Sex*: no information on proportion of males and females
	Age:
	intervention: 36.6 (SD: 18.7) years
	control: 36.6 (SD: 14) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants presenting at the emergency department with an overdose (confirmed by positive blood test) of benzodiazepines, barbiturates or imipramine. Participants in the intervention and control groups did not differ with regard to: their initial mean Glasgow Coma Scale score: intervention: 9 (SD 4.5); control: 10 (SD 4.5); drugs taken: intervention: 12 benzodiazepines, 2 barbiturates and 3 imipramine; control: 13 benzodiazepines, 1 barbiturates and 5 imipramine
	Inclusion criteria: overdose of benzodiazepines, barbiturates or imipramine. Confirmed blood toxicology test
Interventions	*Intervention arm*:
	Type: AC-sorbitol, in addition to usual care (gastric lavage), delivered via nasogastric tube
	Timing: immediately after gastric lavage
	Dose: 1 g/kg AC in a 70% sorbitol solution
	Frequency: 1×

Passeron 1989 *(Continued)*

Integrity: no information

Control arm:

Type: usual care, consisting of gastric lavage, forced diuresis and supportive treatment of symptoms

Timing: NA

Dose: NA

Frequency: NA

Integrity: NA

Outcomes	*Type (unit)*:
	Glasgow Coma Scale
	Blood pressure
	Heart rhythm
	Serum levels of benzodiazepines, barbiturates and imipramine (µg/mL): evolution & proportion with increasing levels) (data not extracted)
	Side effects of the intervention: gastrointestinal issues, pulmonary complications, electrolyte balance (measured via ionogram, glycemia and acidosis)
	Timing:
	Glasgow Coma Scale: at 0 h, 3 h, 9 h, 24 h and 48 h after treatment (intermediate)
	Serum drug levels, blood pressure, heart rhythm, and side effects at 0 h, 3 h and 9 h after treatment (early)
Funding	No information
Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on randomization process
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No information on blinding, but blinding not possible due to differences in treatments. May affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding, might influence assessment of outcomes, such as Glasgow Coma Scale
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Certain patients did not have a blood sample taken at 9 h." Comment: 7 (44%) and 2 (13%) patients in control and intervention group did not have a blood sample at 9 h

Passeron 1989 *(Continued)*

Selective reporting (reporting bias)	High risk	Not reporting the normal pharmacokinetic outcomes, incomplete reporting of basically every outcome reported, no further reporting of the pre-specified outcomes heart rhythm and pulse pressure
Other bias	Low risk	No other risk of bias detected

Pond 1995

Methods	*Study design*: randomized controlled trial
	Study duration: recruitment period from 4 January 1988 to 11 June 1990 (29 months)
	Setting: hospital setting: emergency department of a tertiary referral hospital (Princess Alexandra Hospital, Brisbane)
	Country: Australia
	Number of individuals randomized: 876
	Number of individuals receiving the intervention: 459 (ipecac or lavage)
	Ipecac: 220
	Gastric lavage: 209
	Number of individuals receiving the control: 417 (charcoal, oral or nasogastrically)
	AC: 274
	Nasogastric tube: 133
	Number of individuals lost to follow-up: 82
	Sample size calculated: post hoc power calculation
Participants	*Sex*: 377 males and 499 females
	Age: male: 30 (SD 11; range 14-82 years); female: 30 (SD 1; range 13-81 years)
	Intervention: 30 (SD 12 years (range 13-76 years)
	Control: 31 (SD 13 years; range 13-82 years)
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning:
	Participants presenting within 12 h of drug overdose (adsorbing to AC) whether accidental, intended or during recreational use, at the emergency department. Most presented earlier (140 < 1 h). 59% ingested more than 1 drug
	Ingestion of paracetamol, salicylate, phenothiazines or ethanol, or other drugs
	Inclusion criteria: history of drug overdose, whether accidental, intended or recreational, > 13 years old
	Exclusion criteria: ingestion > 12 h before presentation, treated in a way breaching the protocol, gastric emptying contraindicated, gastric emptying indicated for diagnostic purposes, substance not adsorbed by AC. Confirmation of intoxication by measuring in serum/blood
Interventions	*Intervention arm*:

Type: gastric emptying, being via ipecac in conscious and gastric lavage in obtunted participants. All participants received activated charcoal (Norit "C" Extra) in a slurry with 200 mL sorbitol. AC was given after ipecac-induced vomiting had ceased or after gastric lavage

Timing: before receiving AC-sorbitol

Dose: 30-50 mL ipecac followed by 200 mL water; at least 2 L tap water for gastric lavage, via nasogastric tube

Frequency: 1×, repeated if no vomiting within 30 min

Integrity: no information

Control arm:

Type: activated charcoal-sorbitol + supportive and drug-specific treatment, orally in conscious and via nasogastric tube in obtunted participants

Timing: after diagnosis and allocation to treatment group

Dose: 50 g AC in 200 mL 70% sorbitol slurry

Frequency: 1×

Integrity: no information

Outcomes	*Type (unit)*:
	Proportion with clinical deterioration in the first 6 h after treatment
	Number of days hospitalized (for medical indication related to overdose or its treatment and complications)
	Number of complications
	Admission to ward/ICU
	Timing: clinical course was assessed over the first 6 h at 1-2 h intervals (early)
Funding	No information
Notes	Data for gastric lavage was not extracted, because not within scope of this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Patients were allocated to one of two groups: those who presented on odd-numbered dates to the emptied (E) group; those on even-numbered days to the not-emptied (NE) group." Comment: no adequate randomization
Allocation concealment (selection bias)	High risk	Quote: "Patients were allocated to one of two groups: those who presented on odd-numbered dates to the emptied (E) group; those on even-numbered days to the not-emptied (NE) group." Comment: allocation was not concealed, as randomisation scheme is predictable
Blinding of participants and personnel (performance bias)	High risk	Participants were not blinded (not possible due to difference in interventions); might influence outcomes.

Pond 1995 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding, but might affect assessment of subjective outcomes (clinical deterioration)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Not all participants allocated were treated, but the number remains small (9%) and reasons are thoroughly justified
Selective reporting (reporting bias)	High risk	Certain outcomes (no. referred to wards/ICU, type of complication) only reported for gastric emptying group as a whole, not stratified per treatment
Other bias	Low risk	No other risk of bias detected

Roberts 2006

Methods	*Study design*: randomized controlled trial
	Study duration: recruitment period: 31 March 2002 to October 2004
	Participants were followed up until death/discharge
	Setting: hospital setting: medical wards of 2 Sri Lankan secondary hospitals
	Country: Australia
	Number of individuals randomized: 104
	Number of individuals receiving the intervention: 64
	SDAC: 28
	MDAC: 36
	Number of individuals receiving the control: 40
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*:
	Usual care group: 20 male and 20 female
	SDAC: 8 male and 20 female
	MDAC: 22 male and 14 female
	Age: median (IQR)
	Usual care group:
	21.5 (17.5 to 28.5)
	SDAC: 22 (18.0 to 33.0)
	MDAC: 22.5 (17.5 to 28.0)
	Country (if different from study authors'): Sri Lanka

Roberts 2006 *(Continued)*

	Type, dose and timing of poisoning: participants with acute yellow oleander poisoning, admitted to the medical ward of 3 secondary referral hospitals in Sri Lanka
	Exclusion criteria: < 14 years, pregnant, ingestion of hydrocarbons alone or corrosives, requirement for oral medication, inability to intubate participants with Glasgow coma score < 13, presentation > 72 h postingestion, previous recruitment in the study, previous AC administration for the poisoning episode, < 16 years or unconscious without relatives present to give consent
Interventions	*Intervention arm*:
	Type: SDAC or MDAC in water suspension, in addition to usual care
	Timing: "soon" after admission, for MDAC repeated at 4 h intervals.
	Dose: 50 g superactivated charcoal (Carbomix) in 300 mL water (per dose), administered orally or via nasogastric tube if unconscious
	Frequency:
	SDAC: 1×
	MDAC: 6×
	Integrity: first protocol intended to deliver 18 doses of AC in the multi-dose group, this however was not feasible, so protocol was adapted to 6 doses Compliance was not anticipated a problem as was given while patient was under supervision, however participants was not forced. Analyses were performed intention-to-treat.
	Control arm:
	Type: usual care, consisting of atropine and intravenous fluids, where needed to maintain heart rate > 70 bpm and systolic blood pressure > 80 mmHg. Gastric lavage was initially not planned but upon request of treating physicians was included in standard treatment if participants presented within 2 h of a potentially serious poisoning (3 × 300 mL of water). Furthermore, forced emesis (ipecac) and lavage were mostly performed (54% and 7.5%, respectively) at primary hospitals before transfer to the secondary study hospitals
	Timing: NA
	Dose: NA
	Frequency: NA
	Integrity: NA
Outcomes	*Type (unit)*:
	Primary outcome:
	All-cause hospital mortality
	Secondary outcome:
	Proportion cardiac dysrhythmias requiring anti-digoxin Fab or transfer to tertiary care (3° heart block, Mobitz type II 2° block, sinus bradycardia with heart rate < 35 bpm and sinus arrest or block with sinus pauses > 3 s)
	C_{max} (µg/L)
	T_{max} (µg/L)
	AUC_{0-24} (µg/L × h)
	Gradient of the linear regression time of the concentration/AUC_{0-24} curve (representing elimination) (data not extracted)

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Roberts 2006 *(Continued)*

Mean residence time$_{0-24}$ (h) (data not extracted)

Timing: blood samples were taken at 0 h, 1 h, 4 h, 12 h, 24 h after administration of the first charcoal dose and from then on every 24 h until discharge or death (intermediate)

Funding	National Health and Medical Research Council (Australia), The Welcome trust: grants GR063560MA and GR071669MA.
Notes	This study is part of the Eddleston study, part of the info here comes from the protocol of Eddleston 2008.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were recruited and randomised by a study doctor at the bedside using a dedicated handheld computer at each study hospital. Randomisation occurred after the patient's baseline data had been entered and receipt of consent noted, and could not be manipulated by study doctors. The recruiting doctor was unable to predict allocation before randomisation." Comment: adequate randomization
Allocation concealment (selection bias)	Low risk	Quote: "The recruiting doctor was unable to predict allocation before randomisation." Comment: adequate allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "the primary outcome, vital status at discharge, was unambiguous, and the secondary outcomes were objective; all outcomes were recorded systematically by the study team, not other hospital physicians" Comment: lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the primary outcome, vital status at discharge, was unambiguous, and the secondary outcomes were objective; all outcomes were recorded systematically by the study team, not other hospital physicians". Comment: outcome assessors were kept blinded from data analysis. They were not kept blinded from treatment, but objective outcomes are used.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: data from all eligible participants are reported. Non-eligibility from other participants is thoroughly justified. Quote: "patient follow-up was expected to be near 100% complete; and the analysis will be performed on an intention-to-treat basis."
Selective reporting (reporting bias)	Low risk	All pre-defined outcomes are reported
Other bias	High risk	It is not entirely clear, even to the authors, what exactly is measured with the digoxin assay. The fact that both active cardenolides and (inactive?) metabolites might bind the assay compromise the results of these analyses, as they might explain the wide variability observed. Only participants with 'mild' intoxication were included in this analysis, as the severe cases were treated with Fab or transferred to a tertiary hospital, but these might have shown the biggest effect.

Sue 1994 *(Continued)*

Methods	*Study design*: randomized controlled trial
	Study duration: recruitment period from October 1990 to April 1992
	Setting: hospital setting: emergency department of a children's hospital
	Country: USA
	Number of individuals randomized: 64
	Number of individuals receiving the intervention:
	4 mL/kg group: 16
	6 mL/kg group: 16
	8 mL/kg group: 18
	Number of individuals receiving the control: 14
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: no information
	Age: median age: 25 months (range 3-53 months)
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: children presenting to the emergency department, following a toxic ingestion requiring SDAC
	Exclusion criteria: dehydrated or renal dysfunction and those whose ingestions required MDAC
Interventions	*Intervention arm*:
	Type: activated charcoal + MgCitrate (6%)
	Timing: after appropriate initial care (supportive care, gastric emptying if indicated and diagnostic laboratory evaluation)
	Dose:
	50 g AC in 240 mL, combined with:
	4 mL/kg of MgCitrate (6%) and 2 mL/kg water
	6 mL/kg of MgCitrate (6%)
	8 mL/kg of MgCitrate (6%)
	Frequency: 1×
	Integrity: no attempts were made to control the oral intake of the children following administration of the charcoal slurry
	Control arm:
	Type: activated charcoal
	Timing: after appropriate initial care (supportive care, gastric emptying if indicated and diagnostic laboratory evaluation)
	Dose: 1 g/kg: 50 g AC in 240 mL, combined with 6 mL/kg water

Sue 1994 *(Continued)*

Frequency: 1×

Integrity: no attempts were made to control the oral intake of the children following administration of the charcoal slurry.

Outcomes	*Type (unit)*:
	Time to first stool (h) (data not extracted)
	Number requiring hospitalization
	Number of black-colored stools (data not extracted)
	Potential adverse events (vomiting, diarrhoea, abdominal pain, lethargy)
	Timing: outcomes were measured during the subsequent 48 h after treatment, either by review of the hospital chart or telephone follow-up (intermediate)
Funding	No information
Notes	Only clinically relevant outcome is requirement of hospitalization
	Not clear when outcome hospitalization was measured: after 48 h or initially.
	Study reports "no difference" in diarrhoea, abdominal pain, but no numbers reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on randomization process
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information to support judgment, but lack of blinding may affect outcomes studied
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding, but could affect outcomes studies (e.g. hospitalization)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "No enrolled patient withdrew from the study, and follow-up information was obtained for all children." Comment: adequate
Selective reporting (reporting bias)	High risk	Clinical outcome data are lacking. Adverse events incompletely reported
Other bias	Low risk	No other risk of bias detected

Underhill 1990

Methods	*Study design*: randomized controlled trial

Underhill 1990 *(Continued)*

Study duration: recruitment period between April and October 1988

Setting: hospital setting: accident and emergency departments of two teaching hospitals

Country: UK

Number of individuals randomized: 60

Number of individuals receiving the intervention:

Gastric lavage: 14

Acitvated charcoal: 20

Ipecac: 21

Number of individuals receiving the control: 5

Number of individuals lost to follow-up: 0

Sample size calculated:

Participants	*Sex*: 16 male and 44 female
	Age: mean (range): 25.7 (16-62) years
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: participants presenting within 4 h after an overdose (mean delay: 123 min, range 30-240 min) of at least 5 g paracetamol. 48 took paracetamol without another drug; 21 took paracetamol with alcohol
	Inclusion criteria: > 16 years, presenting < 4 h after intake, ingested > 5 g paracetamol
	Exclusion criteria: depressed conscious level, conditions that might preclude use of any one of the treatment methods
Interventions	*Intervention arm 1*:
	Type: gastric lavage
	Timing: NA
	Dose: NA
	Frequency: NA
	Integrity: NA
	Intervention arm 2:
	Type: activated charcoal (Carbomix)
	Timing: no information
	Dose: AC:Drug ratio of 10:1
	Frequency: 1×
	Integrity: 16 participants managed to take the recommended dose. 4 participants vomited and 1 refused to take more than one mouthful
	Intervention arm 3:
	Type: ipecac
	Timing: no information

Dose: 30 mL

Frequency: 1×, repeated if no vomiting after 30 min

Integrity: mean time to emesis was 20 min (range 5-50), 2 participants did not vomit until 50 min and 2 did not vomit at all

Control arm:

Type: no intervention

Timing: NA

Dose: NA

Frequency: NA

Integrity: NA

Outcomes	*Type (unit)*:
	Plasma paracetamol levels
	Adverse events
	Timing: prior to treatment and 60 min, 90 min and 150 min after the first sample (early)
Funding	No information
Notes	No treatment group was stopped for ethical reasons when the serum paracetamol levels increased between the first and last samples in 4 out of 5 participants.
	Data for gastric lavage was not extracted, because not within scope of this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information on randomization process
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants were not blinded (not possible due to difference in interventions); might influence outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No information on blinding, but should not affect outcome measurements
Incomplete outcome data (attrition bias) All outcomes	Low risk	No indication of incomplete outcomes
Selective reporting (reporting bias)	High risk	No clinical outcomes reported, adverse events incompletely reported
Other bias	Low risk	No other risk of bias detected

Wax 1999

Methods	*Study design*: randomized controlled trial
	Study duration: 27-month recruitment period
	Setting: home setting, with telephone support from a poison centre
	Country: USA
	Number of individuals randomized: 103
	Number of individuals receiving the intervention: 51
	Number of individuals receiving the control: 52
	Number of individuals lost to follow-up: 0
	Sample size calculated: no information
Participants	*Sex*: 57 male and 46 female
	Age: median (range): 2 years (9 months-5 years)
	Country (if different from study authors'): NA
	Type, dose and timing of poisoning: asymptomatic participants with suspected ingestion of a small number (< 6) of potentially toxic berries, including Taxus species (yew), Solanum americanus (nightshade), Ilex species (holly) or unknown berries
	Exclusion criteria: ingestion of a known other type of berry, > 5 berries ingested, symptomatic when calling poison centre, parents planning transport to healthcare facility regardless of the advice of the poison centre, ingestion of more than 1 type of berry/plant parts, contraindication for syrup of ipecac
Interventions	*Intervention arm*:
	Type: syrup of ipecac (+ home observation)
	Timing: no information
	Dose: no information
	Frequency: no information
	Integrity: no information
	Control arm:
	Type: home observation
	Timing: NA
	Dose: NA
	Frequency: NA
	Integrity: NA
Outcomes	*Type (unit)*: symptom assessment (vomiting, diarrhoea, abdominal pain, drowsiness, agitation) and disposition assessment (ED referral, hospital admission)
	Timing: 24 h after telephone call to poison centre (intermediate)
Funding	No information

Wax 1999 *(Continued)*

Notes	—

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "The group who called the poison centre on even days of the month received ipecac followed by parenteral/guardian HO. The group that called the poison centre on odd days of the month were assigned to the HO only group" Comment: not an adequate method of randomization
Allocation concealment (selection bias)	High risk	Randomization method does not allow for allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible to blind, but might affect subjective symptom outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded, which might influence assessment of subjective symptom outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No indication of missing data
Selective reporting (reporting bias)	Low risk	Specified outcomes are reported
Other bias	High risk	Only asymptomatic participants included, no confirmation of actual ingestion and uptake, reporting dichotomous outcomes while measuring using an ordinal scale

AC: activated charcoal; **APACHE**: acute physiology and chronic health evaluation; **AUC**: area under the receiver operating curve; **bpm**: beats per minute; **CBZ**: carbamazepine; **ECG**: electrocardiogram; **ED**: emergency department; **ICU**: intensive care unit; **IQR**: interquartile range; **MDAC**: multi-dose activated charcoal; **NA**: not applicable; **SAPS**: simplified acute physiology score; **SD**: standard deviation; **SDAC**: single-dose activated charcoal; **SEM**: standard error of the mean; **SOI**: syrup of ipecac; **TCA**: tricyclic antidepressant; **UC**: University of California.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Afshari 2010a	Ineligible intervention: IV administration of intervention
Afshari 2010b	Ineligible intervention: IV administration of intervention
Auerbach 1986	Ineligible intervention: comparison between gastric lavage and ipecac
Belon 2007	Ineligible intervention: homeopathic remedy
Berg 1982	Ineligible study population: not oral poisoning
Berlinger 1983	Ineligible population: not oral poisoning

Study	Reason for exclusion
Bhalla 2014	Ineligible intervention: IV administration of intervention
Bosse 1995	Ineligible intervention: not possible to determine the additional effect of activated charcoal on top of hospital treatment
Boxer 1969	Ineligible comparison: hospital treatment vs ipecac
Boyd 1999	Ineligible comparison: 2 types of charcoal compared, no control group without charcoal
Campbell 1992	Ineligible intervention: repeat dose of activated charcoal, no control group without activated charcoal
Chamberlain 1993	Ineligible intervention: different groups received different doses of N-acetylcysteine. Impossible to distinguish the effect of AC from this
Corby 1968	Ineligible intervention: control is apomorphine
Crome 1976	Ineligible intervention: methionine
Dorooshi 2016	Recent trial that was not prospectively registered in a trials register
Eddleston 2009	Ineligible intervention: pralidoxime
Ekins 1987	Ineligible study population: not poisoned patients
Escalante 2016	Recent trial that was not prospectively registered in a trials register
Espinosa 1987	Ineligible intervention: feasibility of administration
Filippone 1987	Ineligible intervention: pre-absorbed durg-charcoal mixture
Fischer 1999	Ineligible comparison: 2 types of charcoal compared, no control group without charcoal
Frenia 1996	Ineligible study population: not oral poisoning
Gomez 1997	Ineligible intervention: pre-absorbed durg-charcoal mixture
Grierson 2000	Ineligible intervention: gastric lavage
Hoegberg 2005	Ineligible intervention: yoghourt
Hoegberg 2012	Ineligible intervention: alcohol
Ilkhanipour 1992	Ineligible study population: not oral poisoning
Ilkhanipour 1993	Ineligible study population: not oral poisoning
IRCT138811142717N1 2010	Ineligible intervention: IV administration of intervention
IRCT20180118038426N2 2018	Recent trial that was not prospectively registered in a trials register. The trial was registered after recruitment had started
Isbister 2011	Ineligible study population: not oral poisoning
ISRCTN50739829 2006	Ineligible intervention: IV administration of treatment

Study	Reason for exclusion
Karim 2001	Ineligible intervention: feasibility of administration
Krenzelok 1985a	Ineligible study population: not poisoning patients
Ly 2004	Ineligible intervention: whole bowel irrigation
MacLean 1973	Ineligible intervention: apomorphine
Mahutte 1983	Ineligible study population: not oral poisoning
Merigian 1988	Ineligible intervention: gastric emptying not specified
Navabi 2017	Ineligible intervention: hospital treatments
Nogue 1987	Ineligible intervention: two formulations of ipecac compared
Olsen 1993	Ineligible intervention: whole bowel irrigation
Olsen 1995	Ineligible intervention: whole bowel irrigation
Pond 1984	Ineligible comparison: no suitable comparison
Roberts 1997	Ineligible intervention: comparison of 2 brands of activated charcoal
Schofferman 1976	Ineligible intervention: apomorphine
Skinner 2012	Ineligible population: chronic poisoning patients
Smith 1967	Ineligible intervention: montmorillonite
Tincu 2017	Recent trial that was not prospectively registered in a trials register
Varipapa 1977	Ineligible study population: not oral poisoning
Vijayakumar 2017	Ineligible intervention: IV administration of intervention
Young 1993	Inelgible comparison: hospital treatment vs ipecac

IV: intravenous.

DATA AND ANALYSES

Comparison 1. SDAC vs no intervention

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Incidence of adverse events	2	476	Peto Odds Ratio (Peto, Fixed, 95% CI)	4.17 [0.30, 57.26]
1.1 Incidence of adverse events	1	451	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Incidence of vomiting	1	25	Peto Odds Ratio (Peto, Fixed, 95% CI)	4.17 [0.30, 57.26]

Analysis 1.1. Comparison 1 SDAC vs no intervention, Outcome 1 Incidence of adverse events.

Study or subgroup	SDAC n/N	No SDAC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
1.1.1 Incidence of adverse events					
Merigian 1990	0/220	0/231			Not estimable
Subtotal (95% CI)	**220**	**231**			**Not estimable**
Total events: 0 (SDAC), 0 (No SDAC)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.1.2 Incidence of vomiting					
Underhill 1990	4/20	0/5		100%	4.17[0.3,57.26]
Subtotal (95% CI)	**20**	**5**		**100%**	**4.17[0.3,57.26]**
Total events: 4 (SDAC), 0 (No SDAC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.07(P=0.29)					
Total (95% CI)	**240**	**236**		**100%**	**4.17[0.3,57.26]**
Total events: 4 (SDAC), 0 (No SDAC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.07(P=0.29)					
Test for subgroup differences: Not applicable					

Favours SDAC   0.01   0.1   1   10   100   Favours no SDAC

Comparison 2. SDAC + hospital intervention vs hospital intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of mortality	2	3425	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.04 [0.79, 1.37]
2 Incidence of adverse events	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Incidence of vomiting	2	1806	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.88, 2.37]
2.2 Incidence of absent bowel sounds	1	3098	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.17, 1.00]
3 Incidence of need for intubation	4	3562	Risk Ratio (M-H, Random, 95% CI)	1.37 [0.76, 2.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Gastric lavage prior to SDAC	2	3175	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.70, 1.27]
3.2 No gastric lavage prior to SDAC	2	387	Risk Ratio (M-H, Random, 95% CI)	2.61 [1.38, 4.93]
4 Incidence of convulsions	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Duration of intubation (h)			Other data	No numeric data
6 AUC ((μg/L) $\times$ h)			Other data	No numeric data
7 C_{max} (μg/L)			Other data	No numeric data
8 T_{max} (h)			Other data	No numeric data
9 Incidence of hospitalization	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10 Incidence of ICU admission	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 1 Incidence of mortality.

Study or subgroup	SDAC n/N	No SDAC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Cooper 2005	0/166	1/161		0.5%	0.13[0,6.61]
Eddleston 2008	109/1544	105/1554		99.5%	1.05[0.79,1.38]
Total (95% CI)	**1710**	**1715**		**100%**	**1.04[0.79,1.37]**
Total events: 109 (SDAC), 106 (No SDAC)					
Heterogeneity: Tau²=0; Chi²=1.07, df=1(P=0.3); I²=6.89%					
Test for overall effect: Z=0.26(P=0.8)					

Favours SDAC   0.005   0.1   1   10   200   Favours no SDAC

Analysis 2.2. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 2 Incidence of adverse events.

Study or subgroup	SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 Incidence of vomiting					
Cooper 2005	25/166	23/161		39.42%	1.05[0.62,1.78]
Merigian 2002	93/404	140/1075		60.58%	1.77[1.4,2.24]
Subtotal (95% CI)	**570**	**1236**		**100%**	**1.44[0.88,2.37]**
Total events: 118 (SDAC), 163 (No SDAC)					
Heterogeneity: Tau²=0.09; Chi²=3.13, df=1(P=0.08); I²=68.02%					

Favours SDAC   0.1   0.2   0.5   1   2   5   10   Favours no SDAC

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Study or subgroup	SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=1.45(P=0.15)					
2.2.2 Incidence of absent bowel sounds					
Eddleston 2008	7/1544	17/1554		100%	0.41[0.17,1]
Subtotal (95% CI)	**1544**	**1554**		**100%**	**0.41[0.17,1]**
Total events: 7 (SDAC), 17 (No SDAC)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.97(P=0.05)					
Test for subgroup differences: Chi²=5.88, df=1 (P=0.02), I²=82.99%					

Favours SDAC 0.1 0.2 0.5 1 2 5 10 Favours no SDAC

Analysis 2.3. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 3 Incidence of need for intubation.

Study or subgroup	Favours SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Gastric lavage prior to SDAC					
Eddleston 2008	73/1544	76/1554		37.7%	0.97[0.71,1.32]
Hultén 1988	7/34	11/43		22.9%	0.8[0.35,1.85]
Subtotal (95% CI)	**1578**	**1597**		**60.61%**	**0.95[0.7,1.27]**
Total events: 80 (Favours SDAC), 87 (No SDAC)					
Heterogeneity: Tau²=0; Chi²=0.16, df=1(P=0.69); I²=0%					
Test for overall effect: Z=0.38(P=0.71)					
2.3.2 No gastric lavage prior to SDAC					
Cooper 2005	8/166	3/161		13.72%	2.59[0.7,9.58]
Merigian 2002	16/28	7/32		25.67%	2.61[1.26,5.42]
Subtotal (95% CI)	**194**	**193**		**39.39%**	**2.61[1.38,4.93]**
Total events: 24 (Favours SDAC), 10 (No SDAC)					
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.99); I²=0%					
Test for overall effect: Z=2.95(P=0)					
Total (95% CI)	**1772**	**1790**		**100%**	**1.37[0.76,2.47]**
Total events: 104 (Favours SDAC), 97 (No SDAC)					
Heterogeneity: Tau²=0.22; Chi²=8.21, df=3(P=0.04); I²=63.45%					
Test for overall effect: Z=1.04(P=0.3)					
Test for subgroup differences: Chi²=8.04, df=1 (P=0), I²=87.56%					

Favours SDAC 0.1 0.2 0.5 1 2 5 10 Favours no SDAC

Analysis 2.4. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 4 Incidence of convulsions.

Study or subgroup	SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Eddleston 2008	13/1544	7/1554		1.87[0.75,4.67]
Hultén 1988	2/34	9/43		0.28[0.06,1.22]

Favours SDAC 0.01 0.1 1 10 100 Favours no SDAC

Analysis 2.5. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 5 Duration of intubation (h).

Study	SDAC	No SDAC	Summary estimate (P value)	# participants
		Duration of intubation (h)		
Eddleston 2008	median (IQR): 112.0 (36.6–234.9)	median (IQR): 88.5 (38.5–203.1)	median difference: 23.5 (P > 0.05)	No information
Merigian 2002	mean: 54.6	mean: 39.9	mean difference: 14.7 (P = 0.70)	No information

Analysis 2.6. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 6 AUC ((μg/L) × h).

Study	SDAC (median (IQR))	no SDAC (median (IQR))	Summary estimate (P value)	# participants
		AUC ((μg/L) × h)		
Roberts 2006	17.7 (11.1;21.8)	19.0 (13.7;24.3)	-1.3 (P > 0.05)	28 vs 40
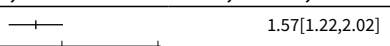
Analysis 2.7. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 7 C_{max} (μg/L).

Study	SDAC (median (IQR))	no SDAC (median (IQR))	Summary estimate (P value)	# participants
		C_{max} (μg/L)		
Roberts 2006	0.98 (0.72;1.50)	1.05 (0.75;1.40)	-0.07 (P > 0.05)	28 vs 40

Analysis 2.8. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 8 T_{max} (h).

Study	SDAC (median (IQR))	no SDAC (median (IQR))	summary estimate (P value)	# participants
		T_{max} (h)		
Roberts 2006	7.2 (5.7;13.8)	12.1 (5.4;17.4)	-4.9 (P > 0.05)	28 vs 40

Analysis 2.9. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 9 Incidence of hospitalization.

Study or subgroup	SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Merigian 2002	79/404	134/1075		1.57[1.22,2.02]

Favours SDAC 0.2 0.5 1 2 5 Favours no SDAC

Analysis 2.10. Comparison 2 SDAC + hospital intervention vs hospital intervention, Outcome 10 Incidence of ICU admission.

Study or subgroup	SDAC n/N	No SDAC n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Merigian 2002	28/404	32/1075		2.33[1.42,3.82]

Favours SDAC 0.2 0.5 1 2 5 Favours no SDAC

Comparison 3.   SDAC vs syrup of ipecac

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Incidence of adverse events	1		Risk Difference (M-H, Random, 95% CI)	Totals not selected
2 Glasgow Coma Scale score	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Mean arterial blood pressure (mmHg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Heart rate (bpm)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Respiratory rate (breaths/min)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 3.1.   Comparison 3 SDAC vs syrup of ipecac, Outcome 1 Incidence of adverse events.

Study or subgroup	Syrup of ipecac n/N	SDAC n/N	Risk Difference M-H, Random, 95% CI	Risk Difference M-H, Random, 95% CI
Amigó Tadín 2002	4/21	2/13		0.04[-0.22,0.29]

Favours SDAC -1 -0.5 0 0.5 1 Favours Syrup of ipecac

Analysis 3.2.   Comparison 3 SDAC vs syrup of ipecac, Outcome 2 Glasgow Coma Scale score.

Study or subgroup	Syrup of ipecac N	Mean(SD)	SDAC N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Amigó Tadín 2002	21	14.8 (0.6)	13	14.9 (0.3)		-0.15[-0.43,0.13]

Favours SDAC -2 -1 0 1 2 Favours Syrup of ipecac

Analysis 3.3.   Comparison 3 SDAC vs syrup of ipecac, Outcome 3 Mean arterial blood pressure (mmHg).

Study or subgroup	Syrup of ipecac N	Mean(SD)	SDAC N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Amigó Tadín 2002	21	87 (14)	13	80 (16)		7[-3.56,17.56]

Favours SDAC -100 -50 0 50 100 Favours Syrup of ipecac

Analysis 3.4. Comparison 3 SDAC vs syrup of ipecac, Outcome 4 Heart rate (bpm).

Study or subgroup	Syrup of ipecac		SDAC		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Amigó Tadín 2002	21	87.1 (15.9)	13	89.5 (20.8)		-2.39[-15.58,10.8]

Favours Syrup of ipecac -100 -50 0 50 100 Favours SDAC

Analysis 3.5. Comparison 3 SDAC vs syrup of ipecac, Outcome 5 Respiratory rate (breaths/min).

Study or subgroup	Syrup of ipecac		SDAC		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Amigó Tadín 2002	21	19.8 (4.3)	13	18.7 (3.9)		1.12[-1.69,3.93]

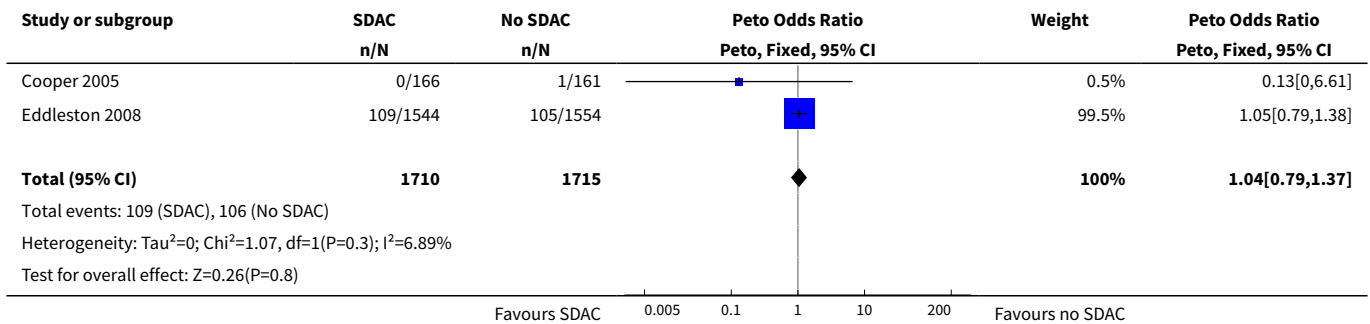Favours Syrup of ipecac -20 -10 0 10 20 Favours SDAC

Comparison 4. MDAC + hospital intervention vs SDAC + hospital intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of mortality	2	3476	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.21, 1.63]
2 Incidence of adverse events	2	3476	Peto Odds Ratio (Peto, Fixed, 95% CI)	3.55 [1.85, 6.79]
3 Incidence of need for cardiac pacing/antitoxin treatment	2	1490	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.02, 4.18]
4 Incidence of life-threatening arrhythmias	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Amount of atropine administered (mg)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6 Number of atropine boluses administered			Other data	No numeric data
7 Incidence of need for intubation	2	3097	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.75, 1.38]
8 Incidence of convulsions	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Duration of coma (h)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10 Duration of intubation (h)			Other data	No numeric data
11 C_{max} (µg/L)			Other data	No numeric data
12 T_{max} (h)			Other data	No numeric data

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13 $T_{1/2}$ (h)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
14 AUC ((μg/L) × h)			Other data	No numeric data
15 Incidence of ICU admission	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 1 Incidence of mortality.
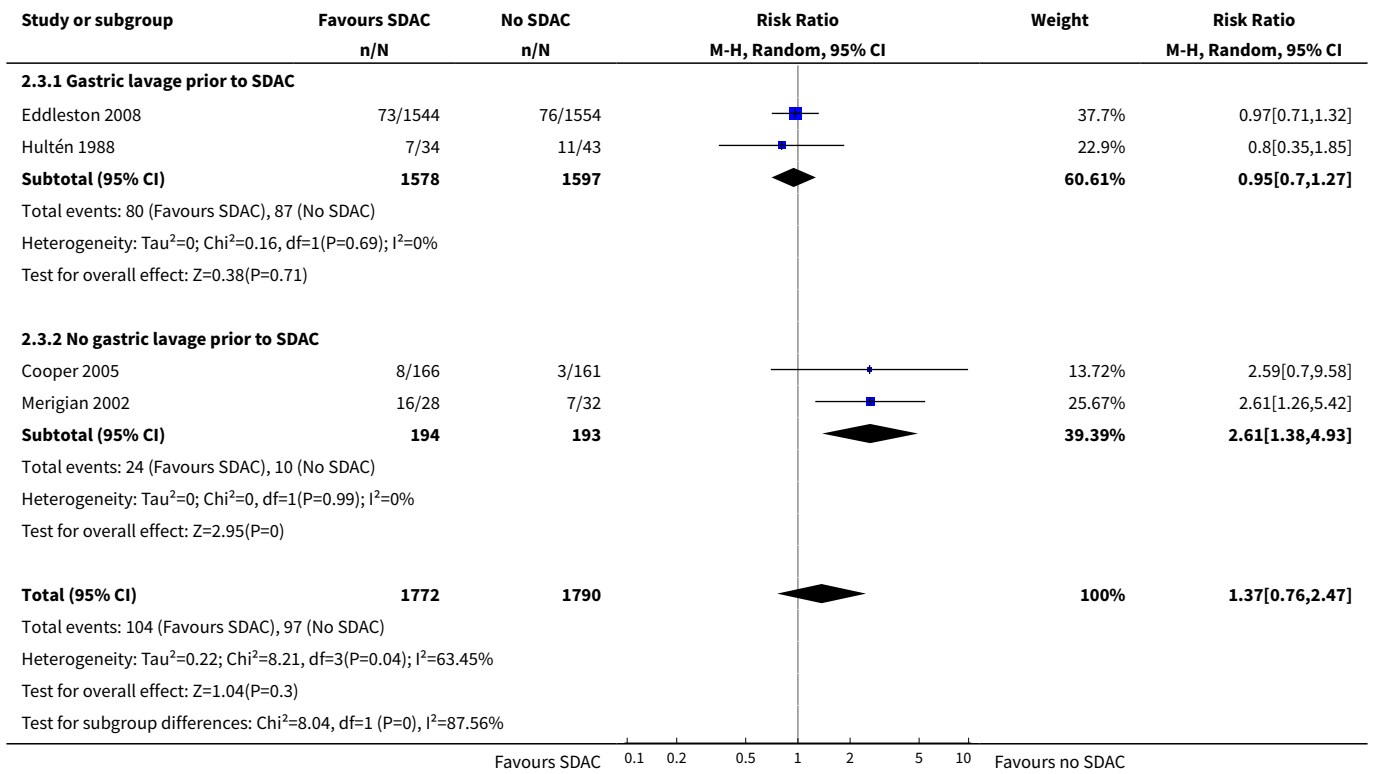
Study or subgroup	MDAC n/N	SDAC n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
De Silva 2003	5/201	16/200		39.61%	0.31[0.12,0.83]
Eddleston 2008	97/1531	109/1544		60.39%	0.9[0.69,1.17]
Total (95% CI)	**1732**	**1744**		**100%**	**0.59[0.21,1.63]**

Total events: 102 (MDAC), 125 (SDAC)

Heterogeneity: Tau²=0.43; Chi²=4.17, df=1(P=0.04); I²=76%

Test for overall effect: Z=1.02(P=0.31)

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours SDAC
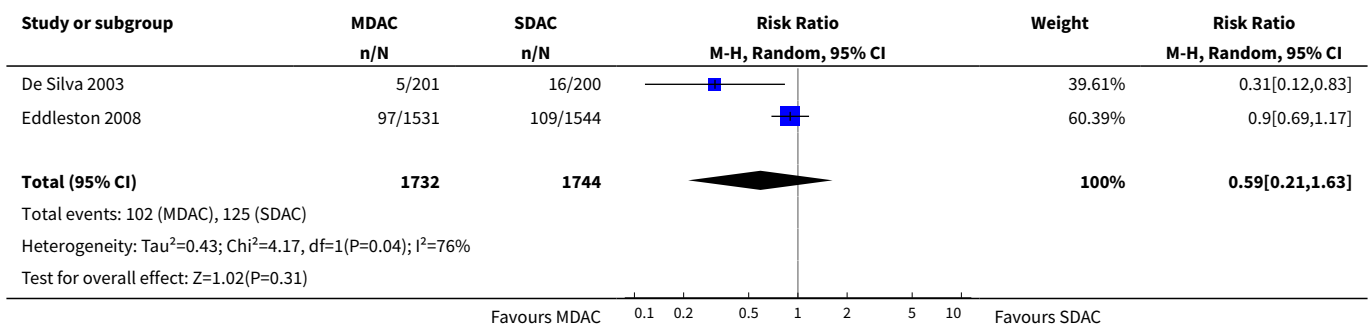
Analysis 4.2. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 2 Incidence of adverse events.

Study or subgroup	MDAC n/N	SDAC n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
De Silva 2003	13/201	0/200		34.61%	7.82[2.59,23.58]
Eddleston 2008	17/1531	7/1544		65.39%	2.34[1.05,5.21]
Total (95% CI)	**1732**	**1744**		**100%**	**3.55[1.85,6.79]**

Total events: 30 (MDAC), 7 (SDAC)

Heterogeneity: Tau²=0; Chi²=3.01, df=1(P=0.08); I²=66.79%

Test for overall effect: Z=3.82(P=0)

Favours MDAC 0.01 0.1 1 10 100 Favours SDAC
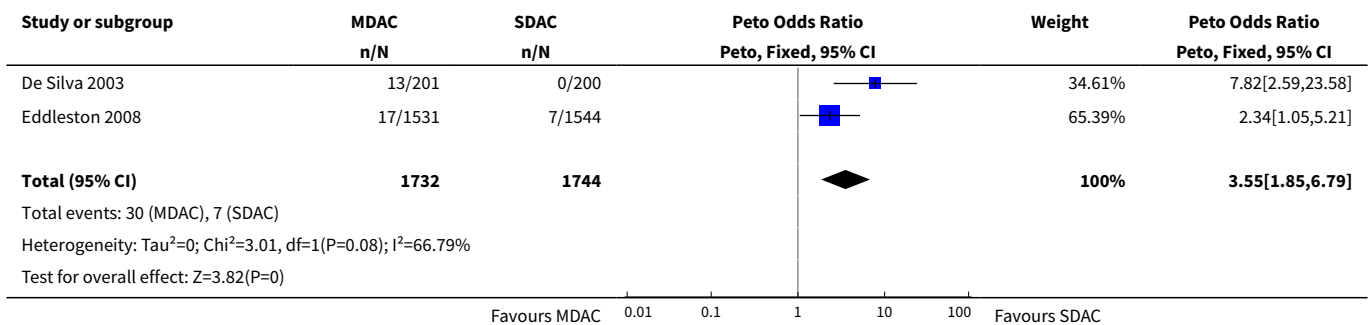
Analysis 4.3. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 3 Incidence of need for cardiac pacing/antitoxin treatment.

Study or subgroup	MDAC n/N	SDAC n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
De Silva 2003	1/201	18/200		43.74%	0.06[0.01,0.41]
Eddleston 2008	85/540	101/549		56.26%	0.86[0.66,1.11]

Favours MDAC 0.002 0.1 1 10 500 Favours SDAC

Study or subgroup	MDAC	SDAC	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Total (95% CI)	741	749		100%	0.26[0.02,4.18]
Total events: 86 (MDAC), 119 (SDAC)					
Heterogeneity: Tau²=3.57; Chi²=7.71, df=1(P=0.01); I²=87.03%					
Test for overall effect: Z=0.95(P=0.34)					

Favours MDAC 0.002 0.1 1 10 500 Favours SDAC

Analysis 4.4. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 4 Incidence of life-threatening arrhythmias.

Study or subgroup	MDAC	SDAC	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
De Silva 2003	3/195	14/190		0.21[0.06,0.71]

Favours MDAC 0.01 0.1 1 10 100 Favours SDAC

Analysis 4.5. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 5 Amount of atropine administered (mg).

Study or subgroup	MDAC		SDAC		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
De Silva 2003	201	3.6 (2.7)	200	5.2 (3.8)		-1.6[-2.25,-0.95]

Favours MDAC -5 -2.5 0 2.5 5 Favours SDAC

Analysis 4.6. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 6 Number of atropine boluses administered.

	Number of atropine boluses administered				
Study	MDAC (median (range))	SDAC (median (range))	Median differ-ence [95% CI]	P value	# participants
De Silva 2003	1 (1-6)	2 (1-12)	0.0 (0.0-1.0)	P < 0.0001	201 vs 200

Analysis 4.7. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 7 Incidence of need for intubation.

Study or subgroup	MDAC	SDAC	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Brahmi 2006	3/6	3/6		7.26%	1[0.32,3.1]
Eddleston 2008	73/1531	73/1554		92.74%	1.02[0.74,1.39]
Total (95% CI)	1537	1560		100%	1.01[0.75,1.38]
Total events: 76 (MDAC), 76 (SDAC)					
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.98); I²=0%					
Test for overall effect: Z=0.09(P=0.93)					

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours SDAC
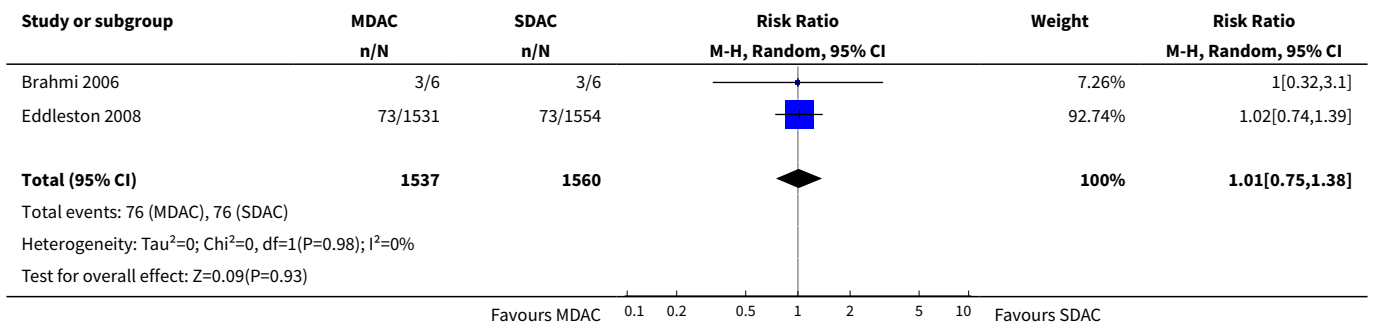
Analysis 4.8.   Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 8 Incidence of convulsions.

Study or subgroup	MDAC n/N	SDAC n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Eddleston 2008	14/1531	13/1554		1.09[0.52,2.32]

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours SDAC
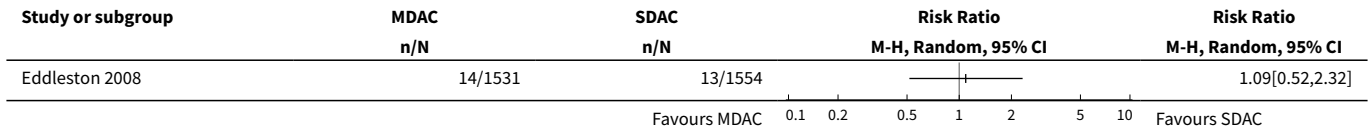
Analysis 4.9.   Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 9 Duration of coma (h).

Study or subgroup	MDAC N	Mean(SD)	SDAC N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Brahmi 2006	3	20.3 (3.1)	3	29.3 (4.1)		-9[-14.79,-3.21]

Favours MDAC -50 -25 0 25 50 Favours SDAC
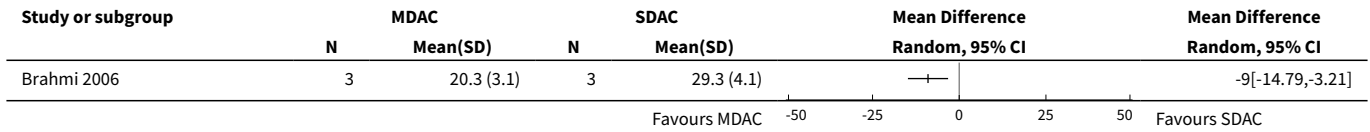
Analysis 4.10.   Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 10 Duration of intubation (h).

Duration of intubation (h)

Study	MDAC	SDAC	Summary estimate	P value	# participants
Brahmi 2006	mean±SD: 24.1±4.2	mean±SD: 36.4±3.6	MD: -12.30, 95%CI [-18.56;-6.04]	P = 0.0001	3 vs 3
Eddleston 2008	median [IQR]: 83.8 (35.0–173.0)	median [IQR]: 112.0 (36.6–234.9)	median difference: -28.2	No information	No information

Analysis 4.11.   Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 11 C_{max} (µg/L).

C_{max} (µg/L)

Study	MDAC	SDAC	Summary estimate	P value	# participants
Brahmi 2006	mean±SD: 33±3.46	mean±SD: 32.6±5.63	MD: 0.40, 95%CI [-4.89;5.69]	P = 0.88	6 vs 6
Roberts 2006	median (IQR): 1.13 (0.86;1.47)	median (IQR): 0.98 (0.72;1.50)	median difference: 0.15	P > 0.05	36 vs 28

Analysis 4.12.   Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 12 T_{max} (h).

T_{max} (h)

Study	MDAC	SDAC	Summary estimate	P value	# participants
Roberts 2006	median (IQR): 8.3 (4.8;15.0)	median (IQR): 7.2 (5.7;13.8)	median difference: 1.1	P > 0.05	36 vs 28

Analysis 4.13. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 13 $T_{1/2}$ (h).

Study or subgroup	MDAC N	MDAC Mean(SD)	SDAC N	SDAC Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Brahmi 2006	6	12.6 (3.5)	6	27.9 (7.4)		-15.32[-21.84,-8.8]

Favours MDAC -50 -25 0 25 50 Favours SDAC

Analysis 4.14. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 14 AUC ((μg/L) × h).

	AUC ((μg/L) × h)				
Study	MDAC	SDAC	Summary estimate	P value	# participants
Roberts 2006	median (IQR): 17.3 (12.8;21.7)	median (IQR): 17.7 (11.1;21.8)	median difference: -0.4	P > 0.05	36 vs 28

Analysis 4.15. Comparison 4 MDAC + hospital intervention vs SDAC + hospital intervention, Outcome 15 Incidence of ICU admission.

Study or subgroup	MDAC n/N	SDAC n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
De Silva 2003	5/201	16/200		0.31[0.12,0.83]

Favours MDAC 0.01 0.1 1 10 100 Favours SDAC

Comparison 5. MDAC + hospital intervention vs hospital intervention

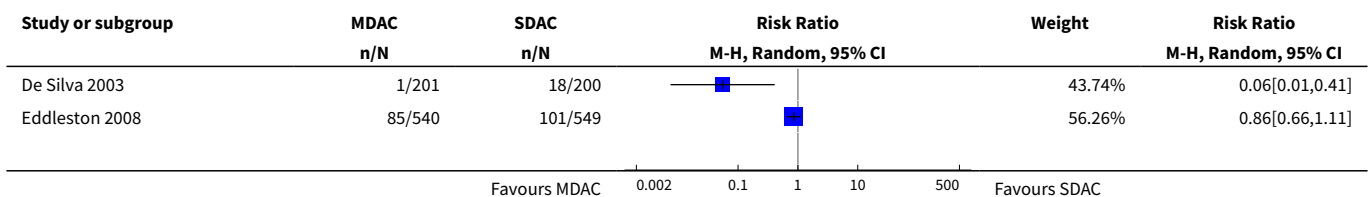| Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of mortality	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Incidence of adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Incidence of need for intubation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Incidence of seizures	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Incidence of need for cardiac pacing/antitoxin treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Length of intubation (h)			Other data	No numeric data
7 AUC			Other data	No numeric data
8 C_{max}			Other data	No numeric data
9 T_{max}			Other data	No numeric data

Analysis 5.1. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 1 Incidence of mortality.

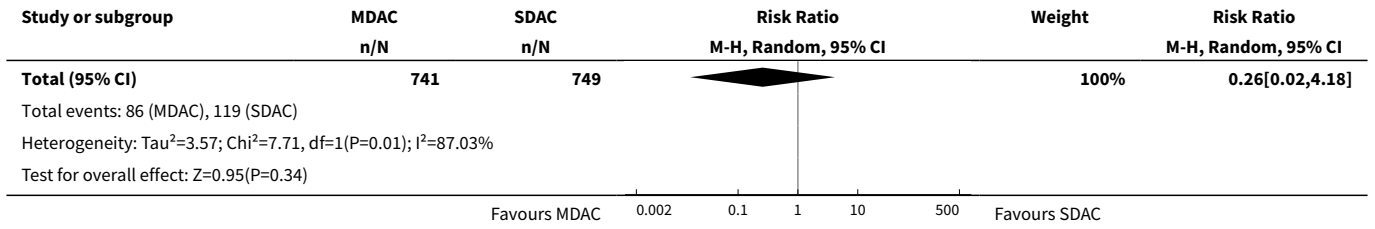| Study or subgroup	MDAC	No intervention	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Eddleston 2008	97/1531	105/1554		0.94[0.72,1.22]

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours no intervention
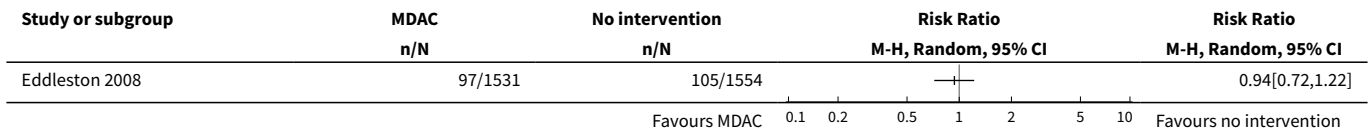
Analysis 5.2. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 2 Incidence of adverse events.

Study or subgroup	MDAC	No intervention	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Eddleston 2008	17/1531	17/1554		1.02[0.52,1.98]

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours no intervention
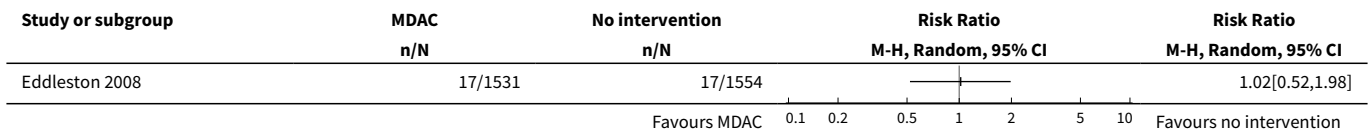
Analysis 5.3. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 3 Incidence of need for intubation.

Study or subgroup	MDAC	No intervention	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Eddleston 2008	73/1531	76/1554		0.97[0.71,1.33]

Favours MDAC 0.1 0.2 0.5 1 2 5 10 Favours no intervention
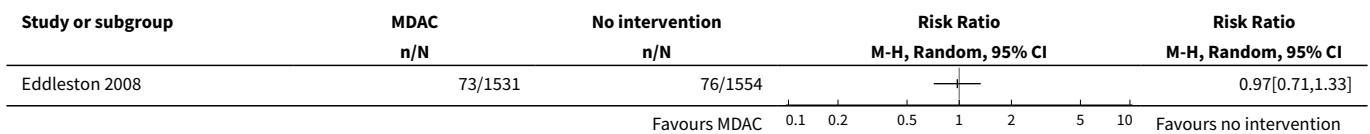
Analysis 5.4. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 4 Incidence of seizures.

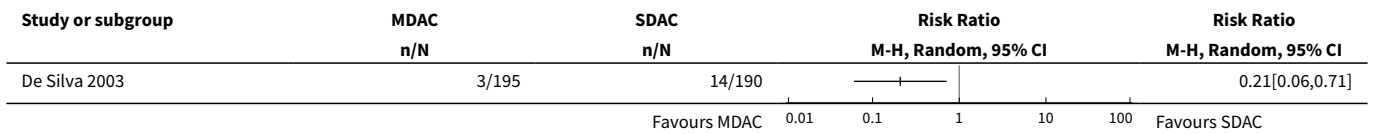| Study or subgroup	MDAC	No intervention	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Eddleston 2008	14/1531	7/1554		2.03[0.82,5.02]

Favours MDAC 0.01 0.1 1 10 100 Favours no intervention
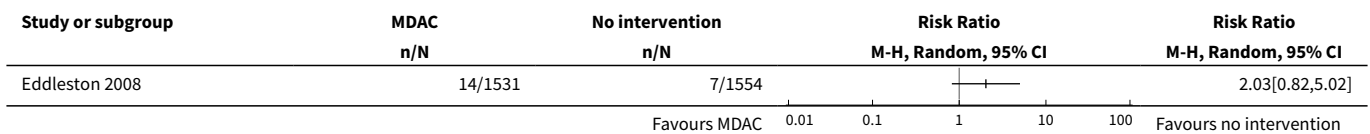
Analysis 5.5. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 5 Incidence of need for cardiac pacing/antitoxin treatment.

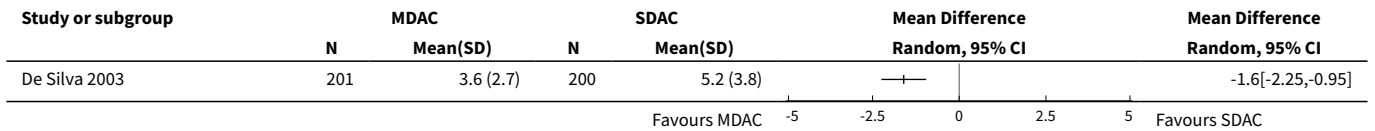| Study or subgroup	MDAC	No intervention	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Eddleston 2008	85/540	101/555		0.86[0.66,1.13]

Favours MDAC 0.2 0.5 1 2 5 Favours no intervention
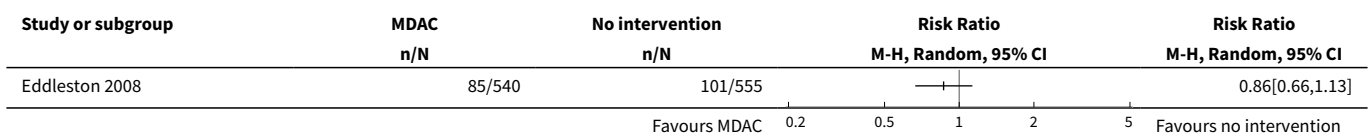
Analysis 5.6. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 6 Length of intubation (h).

Study	MDAC (median IQR)	no intervention (median IQR)	Summary estimate	P value	# participants
		Length of intubation (h)			
Eddleston 2008	83.8 (35.0–173.0)	88.5 (38.5–203.1)	median difference: -4.7	P > 0.05	No information

Analysis 5.7. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 7 AUC.

Study	MDAC (median IQR)	no intervention (median IQR)	Summary estimate	P value	# participants
		AUC			
Roberts 2006	17.3 (12.8;21.7)	19.0 (13.7;24.3)	median difference: -1.7	P > 0.05	36 vs 40

Analysis 5.8. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 8 C_{max}.

Study	MDAC (median IQR)	no intervention (median IQR)	Summary estimate	P value	# participants
		C_{max}			
Roberts 2006	1.13 (0.86;1.47)	1.05 (0.75;1.40)	median difference: 0.08	P > 0.05	36 vs 40
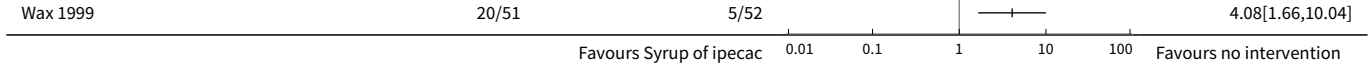
Analysis 5.9. Comparison 5 MDAC + hospital intervention vs hospital intervention, Outcome 9 T_{max}.

Study	MDAC (median IQR)	no intervention (median IQR)	Summary estimate	P value	# participants
		T_{max}			
Roberts 2006	8.3 (4.8;15.0)	12.1 (5.4;17.4)	median difference: -3.8	P > 0.05	36 vs 40

Comparison 6. Syrup of ipecac vs no intervention
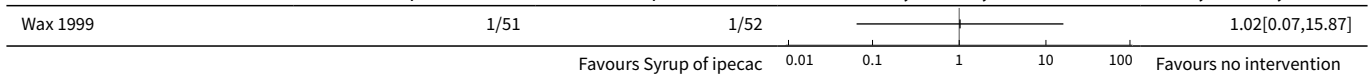
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of diarrhoea	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Incidence of abdominal pain	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Incidence of sedation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Incidence of agitation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Syrup of ipecac vs no intervention, Outcome 1 Incidence of diarrhoea.

Study or subgroup	Syrup of ipecac n/N	No intervention n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wax 1999	20/51	5/52		4.08[1.66,10.04]
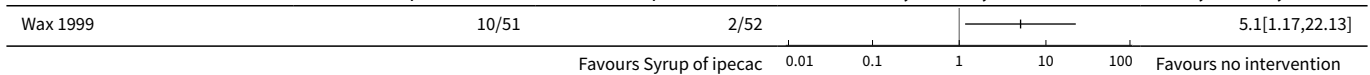
Favours Syrup of ipecac 0.01 0.1 1 10 100 Favours no intervention

Analysis 6.2. Comparison 6 Syrup of ipecac vs no intervention, Outcome 2 Incidence of abdominal pain.

Study or subgroup	Syrup of ipecac n/N	No intervention n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wax 1999	1/51	1/52		1.02[0.07,15.87]
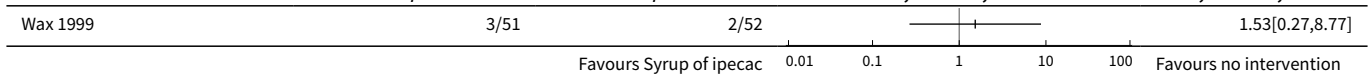
Favours Syrup of ipecac 0.01 0.1 1 10 100 Favours no intervention

Analysis 6.3. Comparison 6 Syrup of ipecac vs no intervention, Outcome 3 Incidence of sedation.

Study or subgroup	Syrup of ipecac n/N	No intervention n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wax 1999	10/51	2/52		5.1[1.17,22.13]

Favours Syrup of ipecac 0.01 0.1 1 10 100 Favours no intervention

Analysis 6.4. Comparison 6 Syrup of ipecac vs no intervention, Outcome 4 Incidence of agitation.

Study or subgroup	Syrup of ipecac n/N	No intervention n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wax 1999	3/51	2/52		1.53[0.27,8.77]

Favours Syrup of ipecac 0.01 0.1 1 10 100 Favours no intervention

Comparison 7. Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of mortality	2		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not selected
2 Incidence of adverse events	3	764	Risk Ratio (M-H, Random, 95% CI)	2.59 [1.37, 4.91]
3 Incidence of clinical improvement	3	989	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.83, 1.21]
4 Incidence of clinical deterioration	2	970	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.46, 1.69]
5 Incidence of hospitalization	3	746	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.17 [0.69, 1.98]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
6 Incidence of ICU admission	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 7.1. Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 1 Incidence of mortality.

Study or subgroup	Syrup of ipecac	No Syrup of ipecac	Peto Odds Ratio	Peto Odds Ratio
	n/N	n/N	Peto, Fixed, 95% CI	Peto, Fixed, 95% CI
Kornberg 1991	0/32	0/38		Not estimable
Kulig 1985	0/241	0/262		Not estimable

Favours SOI 0.01 0.1 1 10 100 Favours no SOI

Analysis 7.2. Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 2 Incidence of adverse events.

Study or subgroup	Syrup of ipecac	no Syrup of ipecac	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Albertson 1989	5/93	1/107		8.5%	5.75[0.68,48.36]
Kornberg 1991	18/32	6/38		46.15%	3.56[1.61,7.89]
Pond 1995	13/220	10/274		45.35%	1.62[0.72,3.62]
Total (95% CI)	**345**	**419**		**100%**	**2.59[1.37,4.91]**

Total events: 36 (Syrup of ipecac), 17 (no Syrup of ipecac)

Heterogeneity: Tau²=0.06; Chi²=2.46, df=2(P=0.29); I²=18.8%

Test for overall effect: Z=2.93(P=0)

Favours SOI 0.01 0.1 1 10 100 Favours no SOI

Analysis 7.3. Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 3 Incidence of clinical improvement.

Study or subgroup	Syrup of ipecac	no Syrup of ipecac	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Kornberg 1991	9/11	7/8		17.7%	0.94[0.64,1.37]
Kulig 1985	211/214	260/262		69.69%	0.99[0.97,1.01]
Pond 1995	29/220	31/274		12.62%	1.17[0.73,1.87]
Total (95% CI)	**445**	**544**		**100%**	**1[0.83,1.21]**

Total events: 249 (Syrup of ipecac), 298 (no Syrup of ipecac)

Heterogeneity: Tau²=0.01; Chi²=3.11, df=2(P=0.21); I²=35.66%

Test for overall effect: Z=0.03(P=0.98)

Favours SOI 0.1 0.2 0.5 1 2 5 10 Favours no SOI

Analysis 7.4.   Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 4 Incidence of clinical deterioration.

Study or subgroup	Syrup of ipecac	no Syrup of ipecac	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Kulig 1985	3/214	2/262		13.41%	1.84[0.31,10.89]
Pond 1995	12/220	19/274		86.59%	0.79[0.39,1.58]
Total (95% CI)	**434**	**536**		**100%**	**0.88[0.46,1.69]**
Total events: 15 (Syrup of ipecac), 21 (no Syrup of ipecac)					
Heterogeneity: Tau²=0; Chi²=0.76, df=1(P=0.38); I²=0%					
Test for overall effect: Z=0.38(P=0.7)					

Favours SOI 0.02 0.1 1 10 50 Favours no SOI

Analysis 7.5.   Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 5 Incidence of hospitalization.

Study or subgroup	Syrup of ipecac	No Syrup of ipecac	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	Peto, Fixed, 95% CI		Peto, Fixed, 95% CI
Albertson 1989	13/93	12/107		39.61%	1.29[0.56,2.97]
Kornberg 1991	3/32	0/38		5.24%	9.51[0.95,95.39]
Kulig 1985	14/214	19/262		55.16%	0.9[0.44,1.82]
Total (95% CI)	**339**	**407**		**100%**	**1.17[0.69,1.98]**
Total events: 30 (Syrup of ipecac), 31 (No Syrup of ipecac)					
Heterogeneity: Tau²=0; Chi²=3.77, df=2(P=0.15); I²=46.89%					
Test for overall effect: Z=0.58(P=0.56)					

Favours SOI 0.005 0.1 1 10 200 Favours no SOI

Analysis 7.6.   Comparison 7 Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic, Outcome 6 Incidence of ICU admission.

Study or subgroup	Syrup of ipecac	No Syrup of ipecac	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI	M-H, Random, 95% CI
Albertson 1989	6/93	5/107		1.38[0.44,4.38]

Favours SOI 0.1 0.2 0.5 1 2 5 10 Favours no SOI
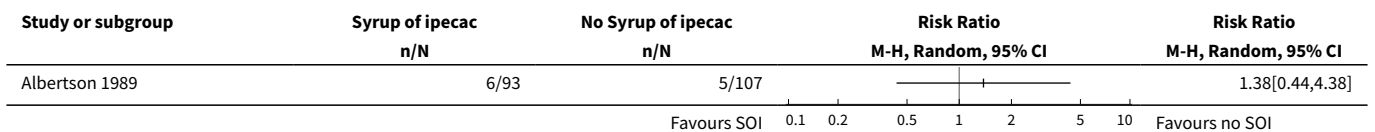
Comparison 8.   SDAC + cathartic vs SDAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of adverse events	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Vomiting	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Lethargy during follow-up	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Incidence of hospitalization	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8 SDAC + cathartic vs SDAC, Outcome 1 Incidence of adverse events.

Study or subgroup	Cathartics n/N	No cathartics n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
8.1.1 Vomiting				
James 1995	23/88	5/28		1.46[0.61,3.49]
8.1.2 Lethargy during follow-up				
Sue 1994	0/50	0/14		Not estimable

Favours Cathartics 0.01 0.1 1 10 100 Favours no cathartics

Analysis 8.2. Comparison 8 SDAC + cathartic vs SDAC, Outcome 2 Incidence of hospitalization.

Study or subgroup	Cathartic n/N	No cathartics n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Sue 1994	3/50	1/14		0.84[0.09,7.46]

Favours Cathartics 0.01 0.1 1 10 100 Favours no cathartics

Comparison 9.   SDAC + cathartic vs SDAC + cathartic (higher dose)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of hospitalization (8 mL vs 6 mL)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 9.1. Comparison 9 SDAC + cathartic vs SDAC + cathartic (higher dose), Outcome 1 Incidence of hospitalization (8 mL vs 6 mL).

Study or subgroup	8 ml cathartic n/N	6 ml cathartic n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Sue 1994	2/18	1/16		1.78[0.18,17.8]

Favours 8 ml cathartic 0.01 0.1 1 10 100 Favours 6 ml cathartic

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Comparison 10.   SDAC + cathartic vs SDAC + cathartic (different type)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Incidence of vomiting (sorbitol vs magnesium sulphate	1		Risk Ratio (M-H, Random, 95% CI)	Totals not select-ed
2 Incidence of vomiting (sorbitol vs magnesium citrate)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not select-ed
3 Incidence of vomiting (magnesium sulphate vs magnesium citrate)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not select-ed

Analysis 10.1.   Comparison 10 SDAC + cathartic vs SDAC + cathartic (different type), Outcome 1 Incidence of vomiting (sorbitol vs magnesium sulphate.

Study or subgroup	Sorbitol n/N	Magnesium sulphate n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
James 1995	13/32	4/23		2.34[0.87,6.25]

Favours Sorbitol   0.01   0.1   1   10   100   Favours MgSO4
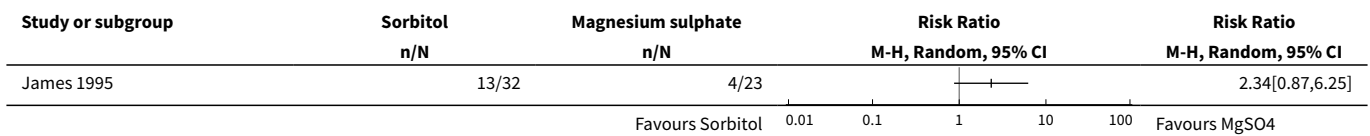
Analysis 10.2.   Comparison 10 SDAC + cathartic vs SDAC + cathartic (different type), Outcome 2 Incidence of vomiting (sorbitol vs magnesium citrate).

Study or subgroup	Sorbitol n/N	Magnesium citrate n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
James 1995	13/32	6/33		2.23[0.97,5.16]

Favours Sorbitol   0.01   0.1   1   10   100   Favours Mg Citrate
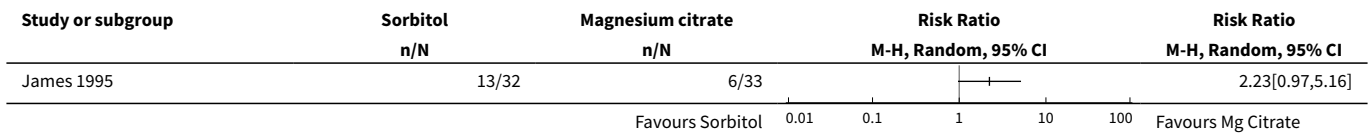
Analysis 10.3.   Comparison 10 SDAC + cathartic vs SDAC + cathartic (different type), Outcome 3 Incidence of vomiting (magnesium sulphate vs magnesium citrate).
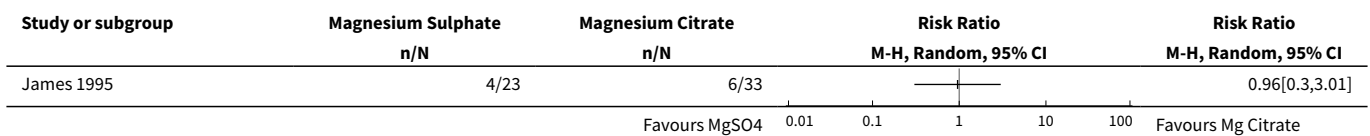
Study or subgroup	Magnesium Sulphate n/N	Magnesium Citrate n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
James 1995	4/23	6/33		0.96[0.3,3.01]

Favours MgSO4   0.01   0.1   1   10   100   Favours Mg Citrate

Comparison 11.   SDAC + cathartic + hospital intervention vs hospital intervention

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Incidence of adverse events	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Totals not select-ed

Analysis 11.1. Comparison 11 SDAC + cathartic + hospital intervention vs hospital intervention, Outcome 1 Incidence of adverse events.

Study or subgroup	SDAC+Cathartic n/N	No intervention n/N	Peto Odds Ratio Peto, Fixed, 95% CI	Peto Odds Ratio Peto, Fixed, 95% CI
Passeron 1989	5/16	0/16		9.94[1.52,65.02]

Favours SDAC+Cathartic 0.01 0.1 1 10 100 Favours no intervention
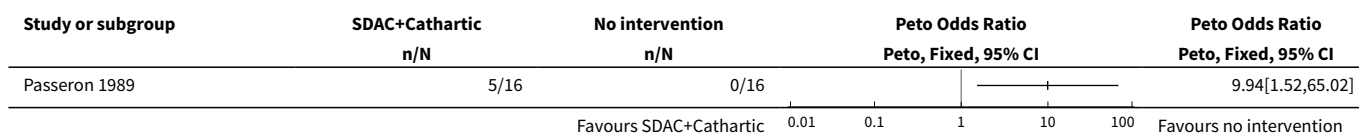
ADDITIONAL TABLES

Table 1. Sources of individual studies

Author and year of publication	Title
Abrass 2012	The evidence for activated charcoal in resource poor settings: a systematic review
American Academy of Clinical Toxicology 1999	Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning
American Academy of Clinical Toxicology 2004	Position paper: cathartics
Chiew 2018	Interventions for paracetamol (acetaminophen) overdoses
Chyka 2005	Position paper: single-dose activated charcoal
Eddleston 2003	Does gastric lavage really push poisons beyond the pylorus? A systematic review of the evidence
Blain 2011	Organophosphorus poisoning (acute)
Höjer 2013	Position paper update: ipecac syrup for gastrointestinal decontamination.
Jones 2002	Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Activated charcoal and gastric absorption of iron compounds
Manoguerra 2005	Guideline on the use of ipecac syrup in the out-of-hospital management of ingested poisons
Qureshi 2011	Adverse effects of activated charcoal used for the treatment of poisoning
Roberts 2011	Enhanced elimination in acute barbiturate poisoning - a systematic review

Table 2. Overview of comparisons

Comparison	Type of poisoning	Study
A. First aid interventions that limit or delay the absorption of the poison in the body		
SDAC vs no intervention	Not specified	Merigian 1990

Table 2. Overview of comparisons *(Continued)*

	Paracetamol	Underhill 1990
SDAC + hospital intervention vs hospital intervention	Not specified	Comstock 1982
	Benzodiazepines + paracetamol or other drug combinations	Cooper 2005
	Tricyclic antidepressants	Crome 1983
	Yellow oleander, organophosphorus/carbamate pesticide, organochlorine, other/unknown pesticide or paraquat, medicine or unknown	Eddleston 2008
	Amitriptyline, clomipramine, mianserin, imipramine, dothiepin, doxepin, nortriptyline, mixed overdoses with most commonly benzodiazepines or alcohol	Hultén 1988
	Not specified	Merigian 2002
	Yellow oleander	Roberts 2006
MDAC + hospital intervention vs SDAC + hospital intervention	Carbamazepine	Behnoush 2009
	Carbamazepine	Brahmi 2006
	Yellow oleander	De Silva 2003
	Yellow oleander, organophosphorus/carbamate pesticide, organochlorine, other/unknown pesticide or paraquat, medicine or unknown	Eddleston 2008
	Yellow oleander	Roberts 2006
SDAC vs syrup of ipecac	Anti-inflammatory drugs, analgesics or psychotropic drugs	Amigó Tadín 2002
MDAC + hospital intervention vs hospital intervention	Benzodiazepine	Bouget 1989
	Yellow oleander, organophosphorus/carbamate pesticide, organochlorine, other/unknown pesticide or paraquat, medicine or unknown	Eddleston 2008
	Yellow oleander	Roberts 2006

B. First aid interventions that evacuate the poison from the gastrointestinal tract

Emetics

Syrup of ipecac vs no intervention	Toxic berries	Wax 1999
Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic	Not specified	Albertson 1989
	Wide variety, most commonly paracetamol	Kornberg 1991
	Not specified	Kulig 1985
	Paracetamol, salicylate, phenothiazines or ethanol, or other drugs	Pond 1995

Table 2.   Overview of comparisons *(Continued)*

Syrup of ipecac 15 mL vs syrup of ipecac 30 mL (dose)	Benzodiazepine tranquillizers or hypnotics, other tranquillizers, other hypnotics, antidepressants, analgesics, antihistamines, miscellaneous drugs and chemicals	Ilett 1977

Cathartics

SDAC + cathartic vs SDAC	Not specified	Sue 1994
SDAC + cathartic vs SDAC	Analgesics, anticonvulsants, antihistamines and decongestants, asthma therapies, automotive products, cardiovascular drugs, gastrointestinal preparations, insecticides, mushrooms, psychotropic drugs, rodenticides, topicals, miscellaneous drugs	James 1995
SDAC + cathartic vs SDAC + cathartic (dose)	Not specified	Sue 1994
SDAC + cathartic vs SDAC + cathartic (type)	Analgesics, anticonvulsants, antihistamines and decongestants, asthma therapies, automotive products, cardiovascular drugs, gastrointestinal preparations, insecticides, mushrooms, psychotropic drugs, rodenticides, topicals, miscellaneous drugs	James 1995

C. Combined first aid interventions that limit uptake and promote evacuation of the poison from the gastrointestinal tract

SDAC + cathartic + hospital intervention vs hospital intervention	Benzodiazepines, barbiturates or imipramine	Passeron 1989
MDAC + cathartic + hospital intervention vs hospital intervention	Paracetamol	Montoya-Cabrera 1999

D. First aid interventions that neutralize or dilute the poison

No studies were identified

APF: Australian Pharmaceutical Formulary; **MDAC**: multi-dose activated charcoal; **SDAC**: single-dose activated charcoal; **USP**: United States Pharmacopeia.

Table 3.   Additional pre-defined outcomes reported in the included studies

A. First aid interventions that limit or delay the absorption of the poison in the body

SDAC vs no intervention

Incidence of clinical deterioration

	SDAC		No intervention		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Merigian 1990	0	220	0	231	Not estimable

Incidence of ICU admission

	SDAC		No intervention		

Table 3. Additional pre-defined outcomes reported in the included studies *(Continued)*

Study	Events	Total	Events	Total	Peto OR (95% CI)
Merigian 1990	0	220	0	231	7.77 (0.15 to 391.93)

SDAC + hospitalintervention vs hospitalintervention

Incidence of clinical deterioration

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Merigian 2002	0	455	0	1075	Not estimable

Grade of coma (4 h after admission)

	SDAC + hospital treatment (N = 9)		Hospital treatment (N = 7)		
Study	Median	IQR	Median	IQR	Median difference (P value)
Crome 1983	2	(1 to 3)	2	(1 to 2.5)	0 (P = 0.55)

Grade of coma (8 h after admission)

	SDAC + hospital treatment (N = 9)		Hospital treatment (N = 7)		
Study	Median	IQR	Median	IQR	Median difference (P value)
Crome 1983	2	(1 to 3)	1	(0.5 to 2)	1 (P = 0.38)

Grade of coma (24 h after admission)

	SDAC + hospital treatment (N = 9)		Hospital treatment (N = 7)		
Study	Median	IQR	Median	IQR	Median difference (P value)
Crome 1983	1	(0 to 2)	0	(0 to 0.5)	1 (P = 0.27)

Incidence of coma grade III (4 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	7	34	6	43	1.48 (0.55 to 3.98)

Incidence of coma grade IV (4 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	1	34	7	43	0.18 (0.02 to 1.40)

Incidence of coma grade III (8 h after admission)

Table 3.   Additional pre-defined outcomes reported in the included studies *(Continued)*

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	2	34	2	43	1.26 (0.19 to 8.52)

Incidence of coma grade IV (8 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	0	34	2	43	0.16 (0.01 to 2.70)

Incidence of coma grade III (24 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Hultén 1988	0	34	0	43	Not estimable

Incidence of coma grade IV (24 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Hultén 1988	0	34	0	43	Not estimable

Incidence of need for cardiac pacing/antitoxin

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Eddleston 2008	101	549	101	555	1.01 (0.79 to 1.30)

Incidence of need for respirator

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	2	34	9	43	0.28 (0.06 to 1.22)

Incidence of systolic blood pressure < 100 mmHg (4 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	4	34	8	43	0.63 (0.21 to 1.92)

Incidence of systolic blood pressure < 100 mmHg (8 h after admission)

Table 3.   Additional pre-defined outcomes reported in the included studies *(Continued)*

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	1	34	5	43	0.25 (0.03 to 2.06)

Incidence of systolic blood pressure < 100 mmHg (24 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	0	34	2	43	0.16 (0.01 to 2.70)

Incidence of heart rate > 100 bpm (4 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	10	34	15	43	0.84 (0.44 to 1.63)

Incidence of heart rate > 100 bpm (8 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	8	34	10	43	1.01 (0.45 to 2.28)

Incidence of heart rate > 100 bpm (24 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	10	34	10	43	1.26 (0.60 to 2.68)

Incidence of cardiac arrhythmias (4 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	1	34	4	43	0.32 (0.04 to 2.70)

Incidence of cardiac arrhythmias (8 h after admission)

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	1	34	3	43	0.42 (0.05 to 3.87)

Incidence of cardiac arrhythmias (24 h after admission)

Table 3. Additional pre-defined outcomes reported in the included studies *(Continued)*

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	1	34	2	43	0.63 (0.06 to 6.68)

Incidence of intubation > 8 h

	SDAC + hospital treatment		Hospital treatment		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	4	34	9	43	0.56 (0.19 to 1.67)

B. First aid interventions that evacuate the poison from the gastrointestinal tract

Syrup of ipecac vs no intervention

Incidence of referrals to the emergency department

	Syrup of ipecac		No intervention		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Wax 1999	1	51	0	52	7.54 (0.15 to 378.83)

Incidence of hospitalizations

	Syrup of ipecac		No intervention		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Wax 1999	0	51	0	52	Not estimable

SDAC + cathartic vs SDAC (higher dose)

Incidence of adverse events (6 mL vs 4 mL)

	SDAC + 6 mL cathartic		SDAC + 4 mL cathartic		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Sue 1994	0	16	0	16	Not estimable

Incidence of adverse events (8 mL vs 4 mL)

	SDAC + 8 mL cathartic		SDAC + 4 mL cathartic		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Sue 1994	0	18	0	16	Not estimable

Incidence of adverse events (8 mL vs 6 mL)

	SDAC + 8 mL cathartic		SDAC + 6 mL cathartic		

Table 3. Additional pre-defined outcomes reported in the included studies *(Continued)*

Study	Events	Total	Events	Total	Peto OR (95% CI)
Sue 1994	0	18	0	16	Not estimable

Incidence of hospitalization (6 mL vs 4 mL)

	SDAC + 6 mL cathartic		SDAC + 4 mL cathartic		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Sue 1994	1	16	0	16	7.39 (0.15 to 372.38)

Incidence of hospitalization (8 mL vs 4 mL)

	SDAC + 8 mL cathartic		SDAC + 4 mL cathartic		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Sue 1994	2	18	0	16	7.01 (0.42 to 117.63)

C. Combined first aid interventions that limit uptake and promote removal of the poison

MDAC + cathartic + hospitalintervention vs hospitalintervention

Incidence of adverse events

	MDAC + cathartic + hospital intervention		Hospital intervention		
Study	Events	Total	Events	Total	Peto OR (95% CI)
Mon-toya-Cabrera 1999	0	7	0	7	Not estimable

$T_{1/2}$ (h)

	MDAC + cathartic + hospital intervention (N = 7)		Hospital intervention (N = 7)		
Study	Mean	SD	Mean	SD	MD (95% CI)
Mon-toya-Cabrera 1999	10	N/A	17	N/A	−7 (not estimable)

bpm: beats per minute; **CI**: confidence interval; **IQR**: interquartile range; **OR**: odds ratio; **RR**: risk ratio; **MDAC**; multi-dose activated charcoal; **SDAC**: single-dose activated charcoal.

Table 4. Pre-defined outcomes that were extracted but not included in the review

A. First aid interventions that limit or delay the absorption of the poison in the body

SDAC vs no intervention

Length of stay in the emergency department (min)

	SDAC			No intervention			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Merigian 1990	252	279	220	230	166	231	22.00 (−20.63 to 64.63)

SDAC + hospitalintervention vs hospitalintervention

Length of ICU stay (h)

	SDAC + hospital intervention			Hospital intervention			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Merigian 2002	54.4	93.15	28	45.5	36.3	32	8.90 (−27.82 to 45.62)

Incidence of ICU stay > 3 days

	SDAC + hospital intervention		Hospital intervention		
Study	Events	Total	Events	Total	RR (95% CI)
Hultén 1988	0	34	5	43	0.11 (0.01 to 2.00)

Length of hospital stay (h)

	SDAC + hospital intervention			Hospital intervention			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Merigian 2002	63.8	79.8	51	91.7	103.97	102	−27.90 (−57.68 to 1.88)
Study	Median	IQR	N	Median	IQR	N	Median difference (P value)
Cooper 2005	6.8	(4.0 to 14.0)	166	5.5	(3.0 to 12.0)	161	1.3 (P = 0.11)

Incidence of hospital stay > 3 days

	SDAC + hospital intervention		Hospital intervention			
Study	Events	Total	Events	Total		RR (95% CI)
Hultén 1988	1	34	4	43		0.32 (0.04 to 2.70)

Length of stay in the emergency department (h)

	SDAC + hospital intervention			Hospital intervention			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Merigian 2002	6.2	3.9	325	5.3	3.9	941	0.90 (0.41 to 1.39)

MDAC + hospitalintervention vs hospitalintervention

Length of hospital stay (h)

	MDAC + hospital intervention			Hospital intervention			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Behnoush 2009	31.0	8.9	30	55.0	8.5	30	−24.00 (−28.40 to −19.60)
Brahmi 2006	30.3	3.4	6	39.7	7.3	6	−9.40 (−15.84 to −2.96)
	Median	IQR	N	Median	IQR	N	Median difference (P value)
De Silva 2003	3	(0.25 to 24)	201	3	(0.5 to 10)	200	0 (P = 0.90)

SDAC vs syrup of ipecac

Length of stay in the emergency department (min)

	Syrup of ipecac			SDAC			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Amigó Tadín 2002	113.21	66.0	21	81.46	27.92	13	31.75 (−0.30 to 63.80)

Table 4.   Pre-defined outcomes that were extracted but not included in the review *(Continued)*

B. First aid interventions that evacuate the poison from the gastrointestinal tract

Syrup of ipecac + SDAC + cathartic vs SDAC + cathartic

Length of hospital stay (days)

	Syrup of ipecac + SDAC + cathartic			SDAC + cathartic			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Albertson 1989	2.4	5.8	13	1.7	5.2	12	0.70 (−3.61 to 5.01)

Length of stay in the emergency department (h)

	Syrup of ipecac + SDAC + cathartic			SDAC + cathartic			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Albertson 1989	6.8	2.9	93	6.0	2.1	107	0.80 (0.09 to 1.51)
Kornberg 1991	4.1	1.1	29	3.4	1.2	38	0.70 (0.15 to 1.25)

Length of ICU stay (h)

	Syrup of ipecac + SDAC + cathartic			SDAC + cathartic			
Study	Mean	SD	N	Mean	SD	N	MD (95% CI)
Albertson 1989	1.8	3.9	6	1.0	0.0	5	Not estimable

CI: confidence interval; **ICU**: intensive care unit; **IQR**: interquartile range; **MD**: mean difference; **SD**: standard deviation; **SDAC**: single-dose activated charcoal.

A P P E N D I C E S

Appendix 1. Search strategies

The Cochrane Library

1. [mh "poisoning"] OR [mh "poisons"] OR poison*:ti,ab,kw OR (toxic NEXT/1 ingestion*):ti,ab,kw OR intoxica*:ti,ab,kw OR overdos*:ti,ab,kw OR [mh "drug overdose"]

2. (active NEXT/1 charcoal):ti,ab,kw OR (activated NEXT/1 charcoal):ti,ab,kw OR (active NEXT/1 carbon):ti,ab,kw OR (activated NEXT/1 carbon):ti,ab,kw OR [mh "charcoal"]

3. [mh "vomiting"] OR vomit*:ti,ab,kw OR emesis:ti,ab,kw OR (gastric NEXT/1 evacuation*):ti,ab,kw OR (gastrointestinal NEXT/1 decontamination*):ti,ab,kw OR [mh "ipecac"] OR ipecac*:ti,ab,kw OR emetic*:ti,ab,kw OR [mh "emetics"] OR [mh "cathartics"] OR cathartic*:ti,ab,kw OR purgative*:ti,ab,kw OR bowel evacuant*:ti,ab,kw OR [mh "sorbitol"] OR sorbitol:ti,ab,kw OR [mh "mannitol"] OR mannitol:ti,ab,kw OR [mh "lactulose"] OR lactulose:ti,ab,kw OR [mh "magnesium sulfate"] OR (magnesium NEXT/1 sulphate):ti,ab,kw OR (magnesium NEXT/1 sulfate):ti,ab,kw OR (magnesium NEXT/1 citrate):ti,ab,kw OR (sodium NEXT/1 sulphate):ti,ab,kw OR (sodium NEXT/1 sulfate):ti,ab,kw

4. ([mh "Drinking"] OR drink*:ti,ab,kw OR intake:ti,ab,kw OR consum*:ti,ab,kw OR ingest*:ti,ab,kw) AND ([mh "drinking water"] OR [mh "water"] OR water:ti,ab,kw)

5. (left NEXT/1 side):ti,ab,kw OR (body NEXT/1 position*):ti,ab,kw OR [mh "posture"] OR posture:ti,ab,kw OR (lateral NEXT/1 decubitus):ti,ab,kw

6. [mh "Milk"] OR milk:ti,ab,kw OR [mh "acetic acid"] OR vinegar:ti,ab,kw OR (acetic NEXT/1 acid):ti,ab,kw OR [mh "citrus"] OR citr*:ti,ab,kw OR orange*:ti,ab,kw OR grapefruit*:ti,ab,kw OR lemon*:ti,ab,kw

7. 2-6 OR

8. 1 AND 7

MEDLINE, using the PubMed interface

1. "poisoning"[MeSH] OR "poisons"[MeSH] OR poison*[TIAB] OR toxic ingestion*[TIAB] OR intoxica*[TIAB] OR overdos*[TIAB] OR "drug overdose"[MeSH]

2. "active charcoal"[TIAB] OR "activated charcoal"[TIAB] OR "active carbon"[TIAB] OR "activated carbon"[TIAB] OR "charcoal"[MeSH]

3. "vomiting"[MeSH] OR vomit*[TIAB] OR emesis[TIAB] OR gastric evacuation*[TIAB] OR gastrointestinal decontamination*[TIAB] OR "ipecac"[MeSH] OR ipecac*[TIAB] OR emetic*[TIAB] OR "emetics"[MeSH] OR "cathartics"[MeSH] OR cathartic*[TIAB] OR purgative*[TIAB] OR bowel evacuant*[TIAB] OR "sorbitol"[MeSH] OR sorbitol[TIAB] OR "mannitol"[MeSH] OR mannitol[TIAB] OR "lactulose"[MeSH] OR lactulose[TIAB] OR "magnesium sulfate"[MeSH] OR "magnesium sulphate"[TIAB] OR "magnesium sulfate"[TIAB] OR "magnesium citrate"[TIAB] OR "sodium sulphate"[TIAB] OR "sodium sulfate"[TIAB]

4. ("Drinking"[Mesh] OR drink*[TIAB] OR intake[TIAB] OR consum*[TIAB] OR ingest*[TIAB]) AND ("drinking water"[MeSH] OR "water"[MeSH] OR water[TIAB])

5. "left side"[TIAB] OR body position*[TIAB] OR "posture"[Mesh] OR posture[TIAB] OR "lateral decubitus"[TIAB]

6. "Milk"[Mesh] OR milk[TIAB] OR "acetic acid"[MeSH] OR vinegar[TIAB] OR "acetic acid"[TIAB] OR "citrus"[MeSH] OR citric*[TIAB] OR citrus*[TIAB] OR orange*[TIAB] OR grapefruit*[TIAB] OR lemon*[TIAB]

7. 2-6 OR

8. (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized[TIAB] OR placebo[TIAB] OR drug therapy[sh] OR randomly[TIAB] OR trial[TIAB] OR groups[TIAB]) NOT (Animals[MeSH] NOT Humans[MeSH])

9. 1 AND 7 AND 8

Embase, using the Embase.com interface

1. 'intoxication'/exp OR 'poison'/exp OR poison*:ab,ti OR (toxic NEXT/1 ingestion*):ab,ti OR intoxica*:ab,ti OR overdos*:ab,ti OR 'drug overdose'/exp

2. 'active charcoal':ab,ti OR 'activated charcoal':ab,ti OR 'active carbon':ab,ti OR 'activated carbon':ab,ti OR 'activated carbon'/exp

3. 'vomiting'/exp OR vomit*:ab,ti OR emesis:ab,ti OR (gastric NEXT/1 evacuation*):ab,ti OR (gastrointestinal NEXT/1 decontamination*):ab,ti OR 'ipecac'/exp OR ipecac*:ab,ti OR emetic*:ab,ti OR 'emetic agent'/exp OR 'laxative'/exp OR cathartic*:ab,ti OR purgative*:ab,ti OR (bowel NEXT/1 evacuant*):ab,ti OR 'sorbitol'/exp OR sorbitol:ab,ti OR 'mannitol'/exp OR mannitol:ab,ti OR 'lactulose'/exp OR lactulose:ab,ti OR 'magnesium sulfate'/exp OR 'magnesium sulphate':ab,ti OR 'magnesium sulfate':ab,ti OR 'magnesium citrate':ab,ti OR 'sodium sulphate':ab,ti OR 'sodium sulfate':ab,ti

4. ('Drinking'/exp OR drink*:ab,ti OR intake:ab,ti OR consum*:ab,ti OR ingest*:ab,ti) AND ('drinking water'/exp OR 'water'/exp OR water:ab,ti)

5. 'left side':ab,ti OR (body NEXT/1 position*):ab,ti OR 'body position'/exp OR posture:ab,ti OR 'lateral decubitus':ab,ti

6. 'milk'/exp OR milk:ab,ti OR 'acetic acid'/exp OR vinegar:ab,ti OR 'acetic acid':ab,ti OR 'citrus'/exp OR citr*:ab,ti OR orange*:ab,ti OR grapefruit*:ab,ti OR lemon*:ab,ti

7. 2-6 OR

8. ('randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross-over':ab,ti OR 'cross over':ab,ti OR (double NEXT/1 blind*):ab,ti OR (single NEXT/1 blind*):ab,ti OR trial:ab,ti OR groups:ab,ti) NOT ('animal'/exp NOT 'human'/exp)

9. 1 AND 7 AND 8

CINAHL, using the EBSCO host interface

1. MH "poisoning+" OR MH "poisons+" OR TI "poison*" OR AB "poison*" OR TI "toxic ingestion*" OR AB "toxic ingestion*" OR TI "intoxica*" OR AB "intoxica*" OR TI "overdos*" OR AB "overdos*" OR MH "overdose"

2. TI "active charcoal" OR AB "active charcoal" OR TI "activated charcoal" OR AB "activated charcoal" OR TI "active carbon" OR AB "active carbon" OR TI "activated carbon" OR AB "activated carbon" OR MH "charcoal"

3. MH "vomiting+" OR TI "vomit*" OR AB "vomit*" OR TI emesis OR AB emesis OR TI "gastric evacuation*" OR AB "gastric evacuation*" OR TI "gastrointestinal decontamination*" OR AB "gastrointestinal decontamination*" OR MH "ipecac" OR TI "ipecac*" OR AB "ipecac*" OR TI "emetic*" OR AB "emetic*" OR MH "emetics+" OR MH "cathartics+" OR TI "cathartic*" OR AB "cathartic*" OR TI "purgative*" OR AB "purgative*" OR TI "bowel evacuant*" OR AB "bowel evacuant*" OR MH "sorbitol" OR TI sorbitol OR AB sorbitol OR MH "mannitol" OR TI mannitol OR AB mannitol OR TI lactulose OR AB lactulose OR MH "magnesium sulfate" OR TI "magnesium sulphate" OR AB "magnesium sulphate" OR TI "magnesium sulfate" OR AB "magnesium sulfate" OR TI "magnesium citrate" OR AB "magnesium citrate" OR TI "sodium sulphate" OR AB "sodium sulphate" OR TI "sodium sulfate" OR AB "sodium sulfate"

4. (TI "drink*" OR AB "drink*" OR TI intake OR AB intake OR TI "consum*" OR AB "consum*" OR TI "ingest*" OR AB "ingest*") AND (MH "Water supply" OR MH "water+" OR TI water OR AB water)

5. TI "left side" OR AB "left side" OR TI "body position*" OR AB "body position*" OR MH "posture+" OR TI posture OR AB posture OR TI "lateral decubitus" OR AB "lateral decubitus"

6. MH "Milk+" OR TI milk OR AB milk OR TI "vinegar" OR AB "vinegar" OR MH "acetic acid" OR MH "citrus+" OR TI "citr*" OR AB "citr*" OR TI "orange*" OR AB "orange*" OR TI "grapefruit*" OR AB "grapefruit*" OR TI "lemon*" OR AB "lemon*"

7. 2-6 OR

8. ((MH "Random Assignment") or (MH "Random Sample+") or (MH "Crossover Design") or (MH "Clinical Trials+") or (MH "Comparative Studies") or (MH "Control (Research)+") or (MH "Control Group") or (MH "Factorial Design") or (MH "Quasi-Experimental Studies+") or (MH "Placebos") or (MH "Meta Analysis") or (MH "Sample Size") or (MH "Research, Nursing") or (MH "Research Question") or (MH "Research Methodology+") or (MH "Evaluation Research+") or (MH "Concurrent Prospective Studies") or (MH "Prospective Studies") or (MH "Nursing Practice, Research-Based") or (MH "Solomon Four-Group Design") or (MH "One-Shot Case Study") or (MH "Pretest-Posttest Design+") or (MH "Static Group Comparison") or (MH "Study Design") or (MH "Clinical Research+")) or (clinical nursing research or random* or cross? over or placebo* or control* or factorial or sham* or meta?analy* or systematic review* or blind* or mask* or trial*)

9. 1 AND 7 AND 8

ISI Web of Science

1. TS=("poison*") OR TS=("toxic ingestion*") OR TS=("intoxica*") OR TS=("overdos*")

2. TS=("active charcoal") OR TS=("activated charcoal") OR TS=("active carbon")

3. TS=("vomit*") OR TS=("emesis") OR TS=("gastric evacuation*") OR TS=("gastrointestinal decontamination*") OR TS=("ipecac") OR TS=("emetic*") OR TS=("cathartic*") OR TS=("purgative*") OR TS=("bowel evacuant*") OR TS=("sorbitol") OR TS=("mannitol") OR TS=("lactulose") OR TS=("magnesium sulphate") OR TS=("magnesium sulfate") OR TS=("magnesium citrate") OR TS=("sodium sulphate") OR TS=("sodium sulfate")

4. (TS=("drink*") OR TS=("intake") OR TS=("consum*") OR TS=("ingest*")) AND (TS=("water"))

5. TS=("left side") OR TS=("body position") OR TS=("posture") OR TS=("lateral decubitus")

6. TS=("milk") OR TS=("acetic acid") OR TS=("vinegar") OR TS=("citr*") OR TS=("orange*") OR TS=("grapefruit*") OR TS=("lemon*")

7. 2-6 OR

8. TS=(clinical trial*) OR TS=(research design) OR TS=(comparative stud*) OR TS=(evaluation stud*) OR TS=(controlled trial*) OR TS=(follow-up stud*) OR TS=(prospective stud*) OR TS=(random*) OR TS=(placebo*) OR TS=(single blind*) OR TS=(double blind*)

9. 1 AND 7 AND 8

International Pharmaceutical Abstracts, using the Ovid interface

1. Poisoning.sh. OR poisons.sh. OR poison*.ti,ab. OR toxic ingestion*.ti,ab. OR intoxica*.ti,ab. OR overdos*.ti,ab. OR (drug overdose).ti,ab.

2. Charcoal.sh. OR carbon.sh. OR active charcoal.ti,ab. OR activated charcoal.ti,ab. OR active carbon.ti,ab. OR activated carbon.ti,ab.

3. Vomiting.sh. OR vomit*.ti,ab. OR emesis.sh. OR emesis.ti,ab. OR gastric evacuation*.ti,ab. OR gastrointestinal decontamination*.ti,ab. OR ipecac.sh. OR ipecac*.ti,ab. OR emetic*.ti,ab. OR emetics.sh. OR cathartics.sh. OR cathartic*.ti,ab. OR purgative*.ti,ab. OR bowel evacuant*.ti,ab. OR sorbitol.sh. OR sorbitol.ti,ab. OR mannitol.sh OR mannitol.ti,ab. OR lactulose.sh. OR lactulose.ti,ab. OR magnesium sulfate.sh. OR magnesium sulphate.ti,ab. OR magnesium sulfate.ti,ab. OR magnesium citrate.sh. OR magnesium citrate.ti,ab. OR sodium sulfate.sh. OR sodium sulphate.ti,ab. OR sodium sulfate.ti,ab.

4. (drink*.ti,ab. OR intake.ti,ab. OR consum*.ti,ab. OR ingest*.ti,ab.) AND (water.sh. OR water.ti,ab.)

5. left side.ti,ab. OR body position*.ti,ab. OR posture.sh. OR posture.ti,ab. OR lateral decubitus.ti,ab.

6. Milk.sh. OR milk.ti,ab. OR acetic acid.sh. OR vinegar.sh. OR vinegar.ti,ab. OR acetic acid.ti,ab. OR citrus.sh. OR citr*.ti,ab. OR orange*.ti,ab. OR grapefruit*.ti,ab. OR lemon*.ti,ab.

7. 2-6 OR

8. 1 AND 7

Clinicaltrials.gov

poisoning OR poison OR poisons OR "toxic ingestion" OR intoxication OR overdose OR overdoses OR overdosing

EU Clinical Trials Register

(poisoning OR poison OR poisons OR "toxic ingestion" OR intoxication OR overdose OR overdoses OR overdosing) AND ("active charcoal" OR "activated charcoal" OR "active carbon" OR Vomiting OR emesis OR emetic OR "gastric evacuation" OR "gastrointestinal decontamination" OR ipecac OR cathartic OR cathartics OR purgative OR purgatives OR "bowel evacuant" OR "bowel evacuants" OR sorbitol OR mannitol OR lactulose OR "magnesium sulphate" OR "magnesium sulfate" OR "magnesium citrate" OR "sodium sulphate" OR "sodium sulfate" OR ((drinking OR drink OR intake OR consuming OR consumption OR ingestion OR ingesting) AND water) OR "left side" OR "body position" OR "body positions" OR posture OR postures OR "lateral decubitus" OR Milk OR "acetic acid" OR vinegar OR citrus OR citric OR orange OR oranges OR grapefruit OR grapefruits OR lemon OR lemons)

WHO International Clinical Trials Registry Platform (ICTRP)

Poison* OR toxic ingestion* OR intoxica* OR overdos*

Appendix 2. Syrup of ipecac + SDAC + cathartic versus SDAC + cathartic for first aid in patients with acute oral poisoning

Syrup of ipecac + SDAC + cathartic versus SDAC + cathartic for first aid in patients with acute oral poisoning
Patient or population: first aid in patients with acute oral poisoning (combination of different drugs or not specified)

(Continued)
Setting: hospital setting
Intervention: syrup of ipecac + single-dose activated charcoal (SDAC) + Cathartic
Comparison: SDAC + Cathartic

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with SDAC + cathartic	**Risk with syrup of ipecac + SDAC + cathartic**				
Incidence of mortality	—	—	—	573 (2 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	The effect was not estimable due to zero events in intervention group (0/300) and control group (0/273). We are uncertain about the effect of syrup of ipecac in addition to SDAC + cathartic on incidence of mortality.
Incidence of adverse events	Study population		RR 2.59 (1.37 to 4.91)	764 (3 RCTs)	⊕⊖⊖⊖ Very low[a,b,c]	We are uncertain about the effect of syrup of ipecac in addition to SDAC + cathartic on incidence of adverse events.
	41 per 1000	105 per 1000 (56 to 199)				
Incidence and severity of symptoms of poisoning: incidence of clinical improvement	Study population		RR 1.00 (0.83 to 1.21)	989 (3 RCTs)	⊕⊕⊖⊖ Low[a,b]	Syrup of ipecac in addition to SDAC + cathartic may make little or no difference in incidence of clinical improvement.
	548 per 1000	548 per 1000 (455 to 663)				
Duration of toxic symptoms	No studies collected or reported this outcome					
Drug absorption	No studies collected or reported this outcome					
Incidence of hospitalization	76 per 1000	89 per 1000 (53 to 151)	Peto OR 1.17 (0.69 to 1.98)	746 (3 RCTs)	⊕⊖⊖⊖ Very low[a,b,d]	We are uncertain about the effect of Syrup of ipecac in addition to SDAC + cathartic on incidence of hospitalization
Incidence of ICU admission	47 per 1000	64 per 1000 (21 to 205)	RR 1.38 (0.44 to 4.38)	200 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,d]	We are uncertain about the effect of Syrup of ipecac in addition to SDAC + cathartic on incidence of ICU admission

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **ICU**: intensive care unit; **RCT**: randomized controlled trial; **RR**: risk ratio; **OR**: odds ratio; **SDAC**: single-dose activated charcoal.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

(Continued)

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

aDowngraded one level for serious limitations in study design: high risk of selection bias and high or unclear risk of detection bias.
bDowngraded one level for serious indirectness: study conducted in a hospital setting.
cDowngraded one level for serious imprecision: low number of events.
dDowngraded one level for serious imprecision: low number of events and wide confidence interval.

Appendix 3. SDAC + cathartic versus SDAC for first aid in patients with acute oral poisoning

SDAC + cathartic versus SDAC for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (not specified or a combination of different drugs)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC) + cathartic
Comparison: SDAC

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with SDAC	**Risk with SDAC + cathartic**				
Incidence of mortality	No studies collected or reported this outcome					
Incidence of adverse events	Study population		RR 1.46 (0.61 to 3.49)	180 (2 RCTs)	⊕⊖⊖⊖ Very lowa,b,c	We are uncertain about the effect of SDAC + cathartic, compared to SDAC alone on the incidence of adverse events.
	119 per 1000	174 per 1000 (73 to 415)				
Incidence and severity of symptoms of poisoning - not reported	No studies looked at this outcome					
Duration of toxic symptoms	No studies collected or reported this outcome					
Drug absorption	No studies collected or reported this outcome					
Incidence of hospitalization	Study population		RR 0.84 (0.09 to 7.46)	64 (1 RCT)	⊕⊖⊖⊖ Very lowa,b,c	We are uncertain about the effect of SDAC + cathartic, compared to SDAC alone on the incidence of ICU admission.
	71 per 1000	60 per 1000 (6 to 533)				
Incidence of ICU admission	No studies collected or reported this outcome					

(Continued)

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **ICU**: intensive care unit; **RCT**: randomized controlled trial; **RR**: risk ratio; **SDAC**: single-dose activated charcoal.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

[a]Downgraded one level for serious study limitations: high risk of reporting bias.
[b]Downgraded one level for serious indirectness: study was conducted in a hospital setting.
[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

Appendix 4. SDAC + cathartic compared to SDAC + cathartic (higher dose) for first aid in patients with acute oral poisoning

SDAC + cathartic compared to SDAC + cathartic (higher dose) for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (not specified)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC) + Cathartic
Comparison: SDAC + Cathartic (higher dose)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with SDAC + cathartic (higher dose)	**Risk with SDAC + cathartic**				
Incidence of mortality	No studies collected or reported this outcome					
Incidence of adverse events: 8 mL vs 4 mL magnesium citrate	—	—	—	34 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,c]	The effect was not estimable due to zero events in intervention group (0/18) and control group (0/16). We are uncertain about the effects of SDAC + cathartic (higher dose) on the incidence of adverse events.
Occurrence and severity of symptoms of poisoning	No studies collected or reported this outcome					

(Continued)

Duration of toxic symptoms	No studies collected or reported this outcome
Drug absorption	No studies collected or reported this outcome

Incidence of hospitalization (8 mL vs 4 mL magnesium citrate)	control:0/16 and intervention 2/18 (Peto OR 7.01, 95% CI 0.42 to 117.63).	—	34 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,d]	We are uncertain about the effects of SDAC + cathartic (higher dose) on the incidence of hospitalization.
Incidence of ICU admission	No studies collected or reported this outcome				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).*

CI: confidence interval; **RCT**: randomized controlled trial; **OR**: odds ratio; **SDAC**: single-dose activated charcoal;

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

[a]Downgraded one level for serious limitations in study design: high risk of reporting bias.
[b]Downgraded one level for serious indirectness: study was conducted in a hospital setting.
[c]Downgraded one level for serious imprecision: low number of events.
[d]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

Appendix 5. SDAC + cathartic compared to SDAC + cathartic (different type) for first aid in patients with acute oral poisoning

SDAC + cathartic compared to SDAC + cathartic (different type) for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (combination of different drugs)
Setting: hospital setting
Intervention: single-dose activated charcoal (SDAC) + cathartic
Comparison: SDAC + cathartic (different type)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with SDAC + Cathartic (different type)	**Risk with SDAC + Cathartic**				
Incidence of mortality	No studies collected or reported this outcome					

(Continued)

Incidence of adverse events: vomiting (sorbitol vs magnesium citrate)	Study population		RR 2.23 (0.97 to 5.16)	65 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,c]	We are uncertain about the effect of different types of cathartics combined with SDAC on the incidence of adverse events.
	182 per 1000	405 per 1000 (176 to 938)				
Incidence and severity of symptoms of poisoning - not reported	No studies collected or reported this outcome					
Duration of toxic symptoms	No studies collected or reported this outcome					
Drug absorption	No studies collected or reported this outcome					
Incidence of hospitalization admission	No studies collected or reported this outcome					
Incidence of ICU admission	No studies collected or reported this outcome					

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **ICU**: intensive care unit; **RR**: risk ratio; **RCT**: randomized controlled trial; **SDAC**: single-dose activated charcoal.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

[a]Downgraded one level for serious study limitations: high risk of reporting bias.
[b]Downgraded one level for serious indirectness: study was conducted in a hospital setting.
[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.

Appendix 6. SDAC + cathartic + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning

SDAC + cathartic + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning			
Patient or population: first aid in patients with acute oral poisoning **Setting**: hospital setting **Intervention**: SDAC + cathartic + hospital intervention **Comparison**: hospital intervention			
Outcomes	**Impact**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**

(Continued)

Incidence of mortality	No studies collected or reported this outcome		
Incidence of adverse events	Control group: 0/16 and intervention group: 5/16 (Peto OR 9.94, 95% CI 1.52 to 65.02). We are uncertain of the effect of SDAC + cathartic on the incidence of adverse events.	32 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,c]
Incidence and severity of symptoms of poisoning: level of coma assessed with: Glasgow Coma Scale Follow-up: 2 days	No numeric data were provided about Glasgow Coma Scale scores, but the course of the scores was reported not to differ significantly between treatments (P = 0.49). We are uncertain of the effect of SDAC + cathartic on the level of coma.	32 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,d]
Duration of toxic symptoms	No studies collected or reported this outcome		
Drug absorption	No studies collected or reported this outcome		
Hospitalization	No studies collected or reported this outcome		
ICU admission	No studies collected or reported this outcome		

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU**: intensive care unit; **OR**: odds ratio; **RCT**: randomized controlled trial; **SDAC**: single-dose activated charcoal.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

[a]Downgraded one level for serious study limitations: high risk of selection bias.
[b]Downgraded one level for serious indirectness: study conducted in a hospital setting.
[c]Downgraded one level for serious imprecision: low number of events and wide confidence intervals.
[d]Downgraded one level for serious imprecision: lack of data.

Appendix 7. MDAC + cathartic + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning

MDAC + cathartic + hospital intervention versus hospital intervention for first aid in patients with acute oral poisoning

Patient or population: first aid in patients with acute oral poisoning (paracetamol)
Setting: hospital setting
Intervention: multiple dose of activated charcoal (MDAC) + Cathartic + Hospital intervention
Comparison: hospital intervention

(Continued)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hospital intervention	**Risk with MDAC + cathartic + hospital intervention**				
Incidence of mortality	No studies collected or reported this outcome					
Incidence of adverse events	—		—	14 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,c]	The effect was not estimable due to the absence of events in the intervention (0/7) and the control group (0/7). We are uncertain about the effect of MDAC with a cathartic on the incidence of adverse events.
Incidence and severity of symptoms of poisoning	No studies collected or reported this outcome					
Duration of toxic symptoms	No studies collected or reported this outcome					
Drug absorption: paracetamol: elimination half-life $T_{1/2}$ (h)	The mean drug absorption: paracetamol: elimination half-life $T_{1/2}$ (h) was 17 h	MD 7 h lower	—	14 (1 RCT)	⊕⊖⊖⊖ Very low[a,b,d]	The study reported no standard deviations or other measures of data spread. We are uncertain about the effect of MDAC with a cathartic on paracetamol elimination half-life.
Incidence of hospitalization	No studies collected or reported this outcome					
Incidence of ICU admission	No studies collected or reported this outcome					

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU**: intensive care unit; **MD**: mean difference; **MDAC**: multi-dose activated charcoal; **RCT**: randomized controlled trial.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Footnotes

[a]Downgraded one level due to serious limitations in study design: high risk of other bias: hepatic toxicity marker values suggest a clinically meaningful difference between the two treatment groups.
[b]Downgraded one level due to serious indirectness: study conducted in a hospital setting.
[c]Downgraded one level due to serious imprecision: low number of events.
[d]Downgraded one level due to serious imprecision: lack of data.

WHAT'S NEW

Date	Event	Description
2 July 2019	Amended	Author affiliations amended

HISTORY

Review first published: Issue 12, 2018

Date	Event	Description
19 December 2018	Amended	Minor changes made as requested by a copy editor

CONTRIBUTIONS OF AUTHORS

Bert Avau: co-ordinated the review; selected studies; extracted data; checked the quality of data extraction; analysed and interpreted data; undertook and checked quality assessment; performed statistical analysis; produced the first draft of the review; contributed to writing and editing the review; made an intellectual contribution to the review; wrote to study authors; and approved the final review prior to submission.

Vere Borra: co-ordinated the review; selected studies; extracted data; checked the quality of data extraction; analysed and interpreted data; undertook and checked quality assessment; performed statistical analysis; produced the first draft of the review; contributed to writing and editing the review; made an intellectual contribution to the review; wrote to study authors; and approved the final review prior to submission.

Anne-Catherine Vanhove: extracted data; analysed and interpreted data; contributed to editing the review; made an intellectual contribution to the review; wrote to study authors; and approved the final review prior to submission.

Philippe Vandekerckhove: conceptualized the review; interpreted data; contributed to editing the review; made an intellectual contribution to the review; approved the final review prior to submission.

Peter De Paepe: interpreted data; contributed to editing the review; made an intellectual contribution to the review; approved the final review prior to submission.

Emmy De Buck: conceptualized the review; interpreted data; contributed to editing the review; made an intellectual contribution to the review; approved the final review prior to submission.

DECLARATIONS OF INTEREST

BA, VB, AC, EDB and PV are employees of the Belgian Red Cross and have no further interests to declare. PDP is a specialist in internal medicine and emergency medicine, and is currently head of the emergency department of the Ghent University Hospital (Belgium). Furthermore, he is appointed by the Belgian Federal Health Authorities as Medical Director of East Flanders and a member of the National Council for emergency Medical Services. PDP is professor in clinical pharmacology at the Heymans Institute of Pharmacology at Ghent University (Belgium).

SOURCES OF SUPPORT

Internal sources

- Foundation for Scientific Research of the Belgian Red Cross, Belgium.

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External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Changes from the protocol

In the protocol, we stated that we would include studies performed in poisoning patients as well as studies with healthy volunteers (Avau 2017). During screening of references, it became clear that there were sufficient patient studies available, which led to the decision to only include these. We believe that studies performed in actual oral poisoning patients give better insight into the reality of oral poisoning than studies performed in healthy volunteers, where poisoning is simulated in a controlled setting.

Furthermore, we described mult-dose activated charcoal as the same intervention as single-dose activated charcoal, but with multiple doses of the same intervention. The identified studies made us aware that we should analyse them as different interventions, which we did.

The pre-defined secondary outcome 'drug recovery rate from the body' did not make it to the review, as we had anticipated finding this outcome in studies in healthy volunteers, not in patient studies. As studies in healthy volunteers were no longer within scope of this review, we did not report this outcome. Instead, we subdivided the primary outcome 'incidence and severity of symptoms of poisoning, including mortality' into two separate outcomes, 'incidence and severity of symptoms of poisoning' and 'mortality'.

We also left out two other pre-defined secondary outcomes, 'length of hospital stay' and 'length of ICU stay'. The Cochrane Injuries review group does not consider these outcomes appropriate because they are prone to bias, as they depend on a lot of confounding factors, such as time of death, insurance coverage, patient income, distance from a hospital, hospital admission policy and bed availability, among other factors. As we extracted these outcomes, we present them in Table 4.

For some comparisons, we identified more than 7 outcomes. The outcomes as stated in the protocol were more generally described; however, it became clear that outcomes such as occurrence and severity of poisoning symptoms could include a wide variety of specific outcomes (e.g. incidence of clinical improvement, incidence of intubation requirement, incidence of convulsions) which we could not combine in a meta-analysis due to the differences in the symptoms. As 'Summary of findings' tables include only seven outcomes, we decided, together with a clinical expert (PD), to choose the clinically most relevant outcomes.

For the assessment of the GRADE domain 'limitations in study design', we decided to downgrade the level of the evidence if one of the studies contributing to the outcome was classified as a having a high risk of bias in one or more of the following domains: selection bias, detection bias, attrition bias or other bias. We did not consider domains with unclear risk of bias. The protocol did not clearly state this. Furthermore, we have expanded explanations on our considerations for the assessment of the GRADE domain 'imprecision'.

During the analysis of our data, we encountered dichotomous outcomes with zero events. We decided to analyse these with the Peto OR method instead of the Maentel-Haenzel method in cases where this method is appropriate, according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). In addition, we have further expanded our Methods section concerning the interpretation of I^2 for the assessment of heterogeneity.

In the protocol we anticipated making subgroups of different drugs taken, single versus multiple doses of an intervention and different time points of the interventions. Based on the identified evidence, we decided to create the following subgroups: different drugs taken, different time points of the intervention, co-interventions administered and type of adverse event experienced. We performed no subgroup analysis for single versus multiple doses of an intervention, as it became clear that these should be treated as two different interventions and are therefore different analyses. As for the different time points of the interventions, we did not identify any studies that compared against a control intervention, so we could not perform subgroup analyses.

For practical reasons, we decided to include an extra review author (AV) to help with data extraction of the studies. This person was included as third author of this review.

Methods not implemented

Selection of subsets of participants

Had we encountered a study where only a subset of participants met the eligibility criteria of our review, we would have only extracted data for this relevant subset, if separate data for this subset were available or could be obtained.

Assessment of reporting biases

Had we identified more than 10 studies for the same outcome, we would have used funnel plots to assess possible publication bias. In case of funnel plot asymmetry, we would have considered small-study effects in the meta-analysis (Higgins 2011).

Sensitivity analysis

We would have performed sensitivity analysis by excluding studies with high or unclear risk of bias for sequence generation, allocation concealment, incomplete outcome reporting or other sources of bias and comparing results with the initial analysis, had more than two studies been in the comparison.

We would also have carried out sensitivity analyses had we been required to impute data for some studies to be able to perform a meta-analysis. We would then have excluded the studies with imputed data and compared the results to the initial analysis.

INDEX TERMS

Medical Subject Headings (MeSH)

Acetaminophen [poisoning]; Analgesics, Non-Narcotic [poisoning]; Antidepressive Agents [poisoning]; Antidotes [therapeutic use]; Benzodiazepines [poisoning]; Carbamazepine [poisoning]; Cathartics [therapeutic use]; Charcoal [therapeutic use]; First Aid [*methods]; Fruit [poisoning]; Ipecac [therapeutic use]; Poisoning [etiology] [*therapy]; Publication Bias; Randomized Controlled Trials as Topic; Thevetia [poisoning]

MeSH check words

Humans